Cardiac Hemodynamic Monitoring for the Management of Heart Failure in the Outpatient Setting

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DESCRIPTION

Note: *This policy only addresses the use of these technologies in ambulatory care and outpatient settings.*

A variety of outpatient cardiac hemodynamic monitoring devices are intended to improve quality of life and reduce morbidity for patients with heart failure by decreasing episodes of acute decompensation. Monitors can identify physiologic changes that precede clinical symptoms and thus allow preventive intervention. These devices operate through various mechanisms, including implantable pressure sensors, inert gas rebreathing, and estimation of left ventricular end-diastolic pressure by arterial pressure during the Valsalva maneuver.

Chronic Heart Failure
Patients with chronic heart failure are at risk of developing acute decompensated heart failure, often requiring hospital admission. Patients with a history of acute decompensation have the additional risk of future episodes of decompensation and death. Reasons for the transition from a stable, chronic state to an acute, decompensated state include disease progression, as well as acute events such as coronary ischemia and dysrhythmias. While precipitating factors are frequently not identified, the most common preventable cause is noncompliance with medication and dietary regimens.

Management
Strategies for reducing decompensation, and thus the need for hospitalization, are aimed at early identification of patients at risk for imminent decompensation. Programs for early identification of heart failure are characterized by frequent contact with patients to review signs and symptoms with a health care provider, education, and medication adjustments as appropriate. These encounters may occur face-to-face in the office or at home, or via cellular or computed technology.

Precise measurement of cardiac hemodynamics is often employed in the intensive care setting to carefully manage fluid status in acutely decompensated heart failure. Transthoracic echocardiography, transesophageal echocardiography, and Doppler ultrasound are noninvasive methods for monitoring cardiac output on an intermittent basis for the more stable patient.

The criterion standard for hemodynamic monitoring is pulmonary artery catheters and central venous pressure catheters. However, they are invasive, inaccurate, and inconsistent in predicting fluid responsiveness. Several studies have demonstrated that catheters fail to improve outcomes in critically ill patients and may be associated with harm. To overcome these limitations, multiple techniques and devices have been developed that use complex imaging technology and computer algorithms to estimate fluid responsiveness, volume status, cardiac output and tissue perfusion. Many are intended for use in outpatient settings but can be used in the emergency department, intensive care unit, and operating room. Three methods are reviewed here: implantable pressure monitoring devices, , inert gas rebreathing, and arterial waveform during the Valsalva maneuver. Use of the last 2 is not widespread because of several limitations including use of proprietary technology making it difficult to confirm their validity and lack of large randomized controlled trials to evaluate treatment decisions guided by these hemodynamic monitors.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

Implantable Pulmonary Artery Pressure Monitoring – CardioMEMS Device

Clinical Content and Therapy Purpose
The purpose of the CardioMEMS system in patients who have heart failure is to provide remote monitoring for early symptoms of heart failure to modify therapy and prevent or reduce hospitalization.

Populations
The relevant population(s) of interest is patients with New York Heart Association (NYHA) Class III heart failure who have had a hospitalization in the past year.

Interventions
Left ventricular end-diastolic pressure (LVEDP) can be approximated by direct pressure measurement of an implantable sensor in the pulmonary artery wall or right ventricular outflow tract. The sensor is implanted via right heart catheterization and transmits pressure readings wirelessly to external monitors. One device, the CardioMEMS Champion Heart Failure Monitoring System, has approval from the U.S. Food and Drug Administration (FDA) for the ambulatory management of heart failure patients. The CardioMEMS device is implanted using a heart catheter system fed through the femoral vein and generally requires patients to have an overnight hospital admission for observation after implantation.

Comparators
The comparator of interest is standard clinical care without testing.

Outcomes
The International Consortium for Health Outcomes Measurement has identified 3 domains of outcomes for a standard outcome set for patients with heart failure.[5,]

- Survival and disease control (i.e., mortality)
- Functioning and disease control (i.e., symptom control including dyspnea, fatigue and tiredness, disturbed sleep, and peripheral edema, activities of daily living including health-related quality of life, maximum physical exertion, independence and psychosocial health including depression and anxiety, confidence and self-esteem)

- Burden of care to patient (i.e., hospital visits including admissions and appointments, treatment side effects, complications)

The Heart Failure Association of the European Society of Cardiology has published a consensus document on heart failure outcomes in clinical trials.[6,] They likewise categorize important outcomes for clinical trials as mortality outcomes (all-cause and cause-specific), morbidity and clinical composites (including hospitalizations, worsening of heart failure, implantable cardioverter device shocks) and symptoms and patient-reported outcomes. The consensus document recommends that hospitalization for heart failure be defined as a hospitalization requiring at least an overnight stay caused by substantive worsening of symptoms and/or signs requiring augmentation of therapy. Measurements of maximal oxygen consumption during exercise, the 6-minute walk test, stair climb test, Short Physical Performance Battery or hand-grip strength are functional measures.

Patient-reported outcome measures include the Kansas City Cardiomyopathy Questionnaire, the NYHA Functional Classification, and the Minnesota Living with Heart Failure Questionnaire.

Generally, demonstration of outcomes over a 1-year period is meaningful to assess outcomes for the intervention.

Randomized Controlled Trials

Abraham et al (2011, 2016) have reported on the results of the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial (CHAMPION), a single-blind RCT in which all enrolled patients were implanted with the CardioMEMS device. Patients were randomized to the CardioMEMS group, in which daily uploaded pulmonary artery pressures were used to guide medical therapy, or to the control group, in which daily uploaded pressures were not made available to investigators and patients continued to receive standard of care management, which included drug adjustments in response to patients' clinical signs and symptoms. An independent clinical endpoints committee, blinded to the treatment groups, reviewed abstracted clinical data and determined if hospitalization was related to heart failure hospitalization. The randomized phase ended when the last patient enrolled completed at least 6 months of study follow-up (average, 18 months) and was followed in an open-access phase during which investigators had access to pulmonary artery pressure for all patients (former control and treatment group). The open-access phase lasted for an average of 13 months. In the randomized phase of the trial, if the investigator did not document a medication change in response to an abnormal pulmonary artery pressure elevation, a remote CardioMEMS nurse could send communications to the investigator related to clinical management. No such activity occurred in the nonrandomized phase. Trial characteristics and results are summarized in Tables 2 and 3. The trial met its primary efficacy endpoint, with a statistically significant 28% relative reduction in the rate of heart failure-related hospitalizations at 6 months. However, members of the FDA advisory committee in 2011 were unable to distinguish the effect of the device from the effect of nurse communications, and so the FDA denied approval of CardioMEMS and

requested additional clarification from the manufacturer Subsequently, the FDA held a second advisory committee meeting in 2013 to review additional data (including open-access phase) and address previous concerns related to impact of nurse communication on the CHAMPION trial. The 2 major limitations in the early data were related to the potential impact of nurse communication and lack of treatment effect in women.

The sponsor conducted multiple analyses to address the impact of nurse intervention on heart failure-related hospitalizations. These analyses included: (1) independent auditing of all nurse communication to estimate quantitatively the number of hospitalizations that could have been influenced by nurse communication, (2) using a propensity-based score to match patients in the CardioMEMS group who did not receive nurse communications with those in the control base, (3) comparing whether the new knowledge of pulmonary arterial pressure in the former control during the open-access phase led to reductions in heart failure-related hospitalizations, (4) comparing whether the ongoing access to pulmonary artery pressures in the treatment group during the open-access phase was accompanied by continued reduced rates of heart failure hospitalizations, and (5) comparing whether if similar access to pulmonary artery pressures in the former control group and treatment group during the open-access phase was associated with similar rates of heart failure-related hospitalizations The FDA concluded that all such analyses had methodologic limitations. Propensity matching cannot balance unmeasured characteristics and confounders, and therefore conclusions drawn from propensity analysis were not definitive. While the FDA concluded that the third-party audit of nurse communication was valid, it was difficult to estimate accurately how many heart failure-related hospitalizations were avoided by the nurse communications. The FDA stated that the longitudinal analyses (see points 3 to 5 above) were the most useful regarding supporting device effectiveness. Therefore, only data from analyses 3 to 5 are summarized in Table 4 and discussed next. It is important to acknowledge that all such analyses were post hoc and were conducted with the intent to test the robustness of potentially biased RCT results; therefore, results from these analyses should be evaluated to assess consistency and not as an independent source of evidence to support efficacy. As indicated in Table 4, the longitudinal analyses of individual patient data showed that the device appears to be associated with reducing heart failure-related hospitalization rate. However, there are important trial limitations, notably, subject dropouts were not random, and patient risk profiles could have changed from the randomized phase to the open-access phase. In the open-access phase, 93 (34%) of 270 subjects in the treatment group and 110 (39%) of 280 subjects in the control group remained in the analysis.

According to the FDA documents, the apparent lack of reduction in heart failure-related hospitalization in women resulted from a greater number of deaths among women in the control group early in the trial, and this early mortality resulted in a competing risk for future heart failure hospitalizations. While both the FDA and sponsor conducted multiple analyses to understand device effectiveness in women, the FDA statisticians concluded that such analyses did clearly delineate the limited treatment effect in women. The decrease in heart-failure related hospitalizations observed in the CardioMEMS post-

approval study was also observed in the subgroup analysis of women, which comprised 37.7% of the study population.

Nonrandomized Studies

Shavelle et. al. (2020) reported 1-year outcomes from the open-label, observational, single-arm, post-approval study of CardioMEMS in 1200 patients (37.7% female) across 104 centers in the U.S. with NYHA Class III heart failure and a heart failure-related hospitalization in the prior year. Study visits were planned at 1, 6, 12, 18, and 24 months. The primary efficacy outcome was the difference between rates of adjudicated heart failure-related hospitalization 1 year after compared to 1 year prior to device implantation. The 12-month visit was completed in 875 patients (72.9%). Prior to 1 year, 76 patients (6.3%) withdrew from the study and 186 patients (15.5%) died. The heart failure-related hospitalization rate was significantly lower at 1-year post-implantation (0.54 versus 1.25 events/patient-year; hazard ratio [HR], 0.43; 95% confidence interval [CI], 0.39 to 0.47; P<0.0001). The rate decreases remained significant regardless of the number of pre-enrollment heart failure-related hospitalizations, with a trend towards a more significant benefit in a small subgroup of patients (n=21) with ≥ 5 pre-enrollment heart failure-related hospitalizations. The rate of all-cause hospitalization (ACH) was also significantly lower (1.67 versus 2.28 events/patient-year; HR, 0.73; 95% CI, 0.68 to 0.78; P<0.0001). These results were consistent across subgroups defined by ejection fraction, sex, race, cardiomyopathy cause, and presence or absence of implantable cardiac defibrillator or cardiac resynchronization therapy. The mean rate of daily pressure transmission was 76 ± 24%. Pressure changes differed according to baseline mean pulmonary artery pressure, with the largest decreases observed in patients with baseline pulmonary artery pressure ≥ 35 mmHg (n=550). Pulmonary artery pressure also decreased in the subgroup of patients that died in the year post implantation. During the study, 94.1% of patients had a medication change, with an average of 1.6 medication changes per month. Medication changes related to an increase or decrease in pulmonary artery pressure were implemented in 81.8% and 55.8% of patients, respectively. The primary safety outcome was defined as freedom from device- or system-related complications and pressure sensor failure at 2 years. Two-year safety follow-up has not yet been concluded. At 1 year, freedom from device- or system-related complications was 99.6% (5 events) and freedom from pressure sensor failure was 99.9% (1 event). The nature of these events and the frequency of procedure-related adverse events was not reported. Study interpretation is limited by the lack of a randomized control group and the potential influence of both information and survivor bias. Assessing heart failure-related hospitalizations as a study entry requirement and an endpoint may also reflect a bias of prior hospitalization in favor of any intervention. Notably, 82.8% of patients had a medication change that was unrelated to changes in pulmonary artery pressure (i.e., up titration of neurohormonal modulation in stable patients). Therefore, it is unclear to what degree heart failure-related hospitalization reduction can be explained by a more intensive follow-up and drug up titration plan in the year following implantation. Details regarding the frequency of nursing and/or provider communications were not reported.

Angermann et. al. (2020) published results from the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). This was an industry-sponsored, prospective, observational, non-randomized study designed to assess the safety and feasibility of the CardioMEMS HF system over 12-month follow up in 31 centers across Germany, the Netherlands, and Ireland. A total of 239 patients (22% female) with NYHA class III heart failure and ≥ 1 heart failure-related hospitalization in the prior year were enrolled for remote pulmonary artery pressure-guided heart failure management. Patients were also contacted by nursing staff on a weekly basis during the first month, and biweekly or monthly based on current NYHA class. NYHA class improved in 83 patients (35.5%) and worsened in 4 patients (1.7%) at 12 months. Mean daily adherence to pulmonary artery pressure transmission was 78.1 ± 23.5% (median, 87.6% [interquartile range, 69.4% to 94.9%]). Co-primary outcome measures, 1-year rates of freedom from device- or system-related complications and sensor failure, were 98.3% (95% CI, 95.8 to 100.0) and 99.6% (95% CI, 97.6 to 100), respectively. Twenty-one serious adverse events (8.9%) were reported during 236 implant attempts, of which 4 were categorized as device- or system-related and 21 as procedure-related. Three procedure-related cardiac deaths were reported. The overall 12-month mortality rate was 13.8%, with no device- or system-related deaths. The secondary outcome measures included heart failure-related hospitalization rate at 12 months compared to the prior year before implantation and health-related quality of life. Heart failure-related hospitalizations decreased 62% (0.60 versus 1.55 events/patient year; HR, 0.38; 95% CI, 0.31 to 0.48; P<0.0001). These reductions were consistent across subgroups defined by sex, age, heart failure etiology, device use, ejection fraction, baseline pulmonary artery pressure, and various comorbidities. Patient-reported health-related quality of life outcomes were assessed with the Kansas City Cardiomyopathy Questionnaire (KCCQ), 9-Item Patient Health Questionnaire (PHQ-9), and the EQ-5D-5L. All measures significantly improved at 6 months and were sustained through 12 months. Cumulative medication changes and the average rate of monthly per-patient medication changes were highest in months 0 to 3 postimplant, with diuretics adjusted most often. While the observed heart failure-related hospitalization rate reduction in MEMS-HF is consistent with U.S. experience with the CardioMEMS device, the authors note that study results may have been impacted by information bias, regression to the mean, asymmetrical data handling, and confounding or selection of patients thought to be adherent to remote patient management requirements. Although helpful for evaluating safety and feasibility, prospective registries using historical events for within-patient comparisons cannot provide definitive effectiveness data. The Hemodynamic-GUIDEd Management of Heart Failure (GUIDE-HF) randomized controlled trial of the CardioMEMS device is currently ongoing in the U.S., with a planned enrollment of 3600 patients across 139 centers.

Abraham et. al. (2019) published a retrospective matched cohort study of Medicare beneficiaries who received the CardioMEMS device between 2014 and 2016.[17,] Patients were matched to 1087 controls by demographics, history and timing of heart failure-related hospitalizations, and number of ACH. Propensity scoring based on arrhythmia, hypertension, diabetes, pulmonary disease, and renal disease was used for additional matching. Follow-up was censored at death, ventricular assist device implant, or heart

transplant. At 12 months post implantation, 616 and 784 heart failure-related hospitalizations occurred in the treatment and control cohorts, respectively. Study characteristics and results are summarized in Tables 7 and 8. The rate of heart failure-related hospitalizations was lower in the treatment cohort at 12 months (HR, 0.76; 95% CI, 0.65 to 0.89; P<0.001). Percentage of days lost to heart failure-related hospitalizations (HR, 0.73; 95% CI, 0.64 to 0.84; P<0.001) and ACH or death (HR, 0.77; 95% CI, 0.68 to 0.88; P<0.001) were both significantly lower in the treatment group. The treatment cohort had 241 deaths and 20 ventricular assist device implants or heart transplants; over the same period, the control cohort had 325 deaths and 13 ventricular assist device implants or heart transplants. Mean (standard deviation [SD]) length of hospital stay was 6.6 (6.5) and 6.5 (5.8) days in the control and treatment cohorts, respectively (P =0.70). Mean (SD) total days spent in hospital for heart failure was 3.7 (9.5) and 4.4 (10.3), respectively. The percentage of days lost owing to heart failure-related hospitalization or death was reduced in the treatment cohort (relative risk [RR], 0.73; 95% CI, 0.63 to 0.83). Limitations of this study include lack of medical history data, including ejection fraction, natriuretic peptide levels, renal function, and medication use. Residual confounding by unmeasured covariates remains possible, including the role of heightened health care team involvement in implanted patients.

Desai et. al. (2017) published a retrospective cohort study of Medicare administrative claims data for individuals who received the CardioMEMS device following the FDA approval. Of 1935 Medicare enrollees who underwent implantation of the device, 1114 were continuously enrolled and had evaluable data for at least 6 months before, and following, implantation. A subset of 480 enrollees had complete data for 12 months before and after implantation. Study characteristics and results are summarized in Tables 7 and 8. The cumulative incidence of heart failure-related hospitalizations were significantly lower in the post implantation period than in the preimplantation period at both 6- and 12-month follow-ups. Limitations of this pre-post retrospective study include lack of data on medical history, ejection fraction, indication for implantation and possible confounding due to amplified touchpoints with the health care system necessitated by the device's implantation.

Vaduganathan (2017) analyzed mandatory and voluntary reports of device-related malfunctions reported to the FDA to identify CardioMEMS HF System-related adverse events within the first 3 years of the FDA approval. From among the more than 5500 CardioMEMS implants in the first 3 years, there were 155 adverse event reports covering 177 distinct adverse events for a rate of 2.8%. There were 28 reports of pulmonary artery injury/hemoptysis (0.5%) that included 14 intensive care unit stays, 7 intubations, and 6 deaths. Sensor failure, malfunction, or migration occurred in 46 cases, of which 35 required recalibrations. Compared with a reported 2.8% event rate, the serious adverse event rate in CHAMPION trial was 2.6% with 575 implant attempts, including 1 case of pulmonary artery injury and 2 deaths. Limitation of the current analysis primarily included lack of adjudication and limited clinical data.

Case Series
In 2017, Heywood et. al. reported pulmonary artery pressure data for the first 2000 consecutive patients with at least 6 months of follow-up who were implanted with CardioMEMS. No clinical data were reported except for pulmonary artery measurement. Study characteristics and results are summarized in Tables 9 and 10. The mean age of the cohort enrolled was 70 years and the mean follow-up period was 333 days. There was a median of 1.2 days between remote pressure transmissions and greater than 98% weekly use of the system, demonstrating a high level of adherence.

Section Summary
The pivotal CHAMPION RCT reported a statistically significant decrease in heart failure-related hospitalizations in patients implanted with CardioMEMS device compared with usual care. However, trial results were potentially biased in favor of the treatment group due to use of additional nurse communication to enhance protocol compliance with the device. The trial intended to assess the physician's ability to use pulmonary artery pressure information and not the capabilities of the sponsor's nursing staff to monitor and correct physician-directed therapy. The manufacturer conducted multiple analyses to address the potential bias from the nurse interventions. These analyses were reviewed favorably by the FDA. While these analyses demonstrated the consistency of benefit from the CardioMEMS device, all such analyses have methodologic limitations. With greater adoption of this technology, it is likely to be used by a broader group of clinicians with variable training in the actual procedure and used in patients at a higher risk compared with those in the CHAMPION trial. Early safety data have been suggestive of a higher rate of procedural complications, particularly related to pulmonary artery injury. While the U.S. CardioMEMS post-approval study and European MEMS-HF study reported a significant decrease in heart-failure related hospitalizations with few device- or system-related complications at 1 year, the impact of nursing interventions remains unclear. Complete 2-year safety outcomes from the CardioMEMS post-approval study are pending, and the serious adverse event rate in the MEMS-HF trial was 8.9%. Given that the intervention is invasive and intended to be used for a highly prevalent condition, in the light of limited safety data, lack of demonstrable mortality benefit, and pending questions related to its benefit for reduction in hospitalization, the net benefit remains uncertain. Concerns may be clarified by the ongoing GUIDE-HF RCT that proposes to enroll 3600 patients.

Inert Gas Rebreathing

Clinical Context and Therapy Purpose
The purpose of inert gas breathing in patients who have heart failure in an outpatient setting is: (1) to guide volume management, (2) to identify physiologic changes that precede clinical symptoms and thus allow preventive interventions, and (3) to prevent hospitalizations.

Populations
The relevant population of interest is patients with chronic heart failure who are at risk of developing ADHF.

Interventions
The test being considered is inert gas breathing.
Inert gas rebreathing is based on the observation that the absorption and disappearance of a blood-soluble gas are proportional to cardiac blood flow. The patient is asked to breathe and rebreathe from a bag filled with oxygen mixed with a fixed proportion of 2 inert gases, typically nitrous oxide and sulfur hexafluoride. The nitrous oxide is soluble in blood and is therefore absorbed during the blood's passage through the lungs at a rate proportional to the blood flow. The sulfur hexafluoride is insoluble in blood and therefore stays in the gas phase and is used to determine the lung volume from which the soluble gas is removed. These gases and carbon dioxide are measured continuously and simultaneously at the mouthpiece.

This noninvasive procedure is administered by a cardiologist in an outpatient clinical setting.

Comparators
The comparator of interest is standard clinical care without testing. Decisions on guiding volume management are being made based on signs and symptoms.

Patients with heart failure are managed by cardiologists in an outpatient clinical setting.

Outcomes
The general outcomes of interest are the prevention of decompensation episodes, reduction in hospitalization and mortality, and improvement in quality of life.

Trials of using inert gas rebreathing for this population were not found. Generally, demonstration of outcomes over a 1-year period is meaningful for interventions

Section Summary
No studies on the clinical validity were identified that would establish how the use of inert gas rebreathing measurements helps detect the likelihood of decompensation.

No studies were identified that determined how the use of inert gas rebreathing measurements is associated with changes in patient management or evaluated the effects of this technology on patient outcomes. It is unclear how such devices will improve patient outcomes.

Noninvasive Left Ventricular End-Diastolic Pressure Estimation (*LVEDP)*

Clinical Context and Test Purpose
The purpose of noninvasive left ventricular end-diastolic pressure estimation *(*LVEDP) estimation in patients who have heart failure in an outpatient setting is (1) to guide

volume management, (2) to identify physiologic changes that precede clinical symptoms and thus allow preventive interventions, and (3) to prevent hospitalizations.

Populations
The relevant population of interest is patients with chronic heart failure who are at risk of developing acute decompensated heart failure (ADHF).

Interventions
The test being considered is noninvasive LVEDP estimation.

LVEDP is elevated with acute decompensated heart failure. While direct catheter measurement of LVEDP is possible for patients undergoing cardiac catheterization for diagnostic or therapeutic reasons, its invasive nature precludes outpatient use. Noninvasive measurements of LVEDP have been developed based on the observation that arterial pressure during the strain phase of the Valsalva maneuver may directly reflect the LVEDP. Arterial pressure responses during repeated Valsalva maneuvers can be recorded and analyzed to produce values that correlate to the LVEDP.
This noninvasive procedure is administered by a cardiologist in an outpatient clinical setting.

Comparators
The comparator of interest is standard clinical care without testing. Decisions guiding volume management are being made based on signs and symptoms.
Patients with heart failure are managed by cardiologists in an outpatient clinical setting.

Outcomes
The general outcomes of interest are the prevention of decompensation episodes, reduction in hospitalization and mortality, and improvement in quality of life.

Trials of using noninvasive LVEDP estimation for this population were not found. Generally, demonstration of outcomes over a 1-year period is meaningful for interventions.

Clinically Valid
Silber et. al. (2012) reported on finger photoplethysmography during the Valsalva maneuver performed in 33 patients before cardiac catheterization. LVEDP was measured via a catheter placed in the left ventricle and used as the reference standard. For identifying LVEDP greater than 15 mm Hg, finger photoplethysmography during the Valsalva maneuver was 85% sensitive (95% CI, 54% to 97%) and 80% specific (95% CI, 56% to 93%).

Section Summary
Only 1 study was identified assessing the use of LVEDP monitoring in this patient population; it reported an 85% sensitivity and an 80% specificity to detect LVEDP greater than 15 mm Hg. No studies were identified that determined how the use of

noninvasive LVEDP estimation is associated with changes in patient management or evaluated the effects on patient outcomes.

Computerized Pulse Waveform Analysis

The CV Profilor®DO-2020 CardioVascular Profiling System and the SphygmoCor® Cardiovascular Management System are examples of non-invasive medical devices that provide an indication of arterial compliance (elasticity indices for both large and small arteries), which can be used to determine if patients have potential underlying vascular disease. The devices also measure systolic, diastolic, and mean arterial pressures and pulse rate, and calculates body surface area, body mass index and pulse pressure.

These devices obtain upper-arm blood pressure values and waveform data by non-invasive methods, via the use of an oscillometric blood pressure module and via the application of specially designed equipment.

The acquisition of calibrated radial artery blood pressure waveform data involves, the coordinated use of a blood pressure cuff placed on the left upper-arm and a piezoelectric-based, direct contact, acoustical transducer placed over the right radial artery adjacent to the styloid process of the radius (by the wrist). The cuff systolic and diastolic pressures are utilized to calibrate the radial artery waveform data into units of pressure based on the median high and low value contained in a 30-second collection of blood pressure waveform data.
An embedded computer performs a "pulse contour analysis" of the calibrated, digitized blood pressure waveform data, and generates a report. The clinical data collected and analyzed are accurate and repeatable and can be used in determining hemodynamic parameters relating to the structure, function and changes of a patient's cardiovascular system.

The report summarizes the pulse contour analysis performed on a 30-second collection of the radial artery blood pressure waveforms. The results are based on the use of an electrical analog model which represents the vasculature as consisting of a capacitative compliance element (Large Artery Elasticity Index), an oscillatory or reflective compliance element (Small Artery Elasticity Index), an inductance and a resistance, during the diastolic decay portion of the cardiac cycle.

Summary of Evidence Computerized Pulse Waveform Analysis

No controlled studies were found in the published literature that validates the application of non-invasive medical devices for the measuring of arterial elasticity for cardiovascular disease. No evidence was found to show that evaluation of the status of the arterial elasticity is predictive and, thus, that type of evaluation cannot be used to alter the treatment of individuals. The evidence is insufficient to demonstrate that non-invasive measurements of arterial elasticity alter patient management or improves net health outcomes.

Summary of Evidence

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring with an implantable pulmonary artery pressure sensor device, the evidence includes RCTs. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. One implantable pressure monitor, the CardioMEMS device, has U.S. FDA approval. The pivotal CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients RCT reported a statistically significant decrease in heart failure-related hospitalizations in patients implanted with CardioMEMS device compared with usual care. However, trial results were potentially biased in favor of the treatment group due to use of additional nurse communication to enhance protocol compliance with the device. The manufacturer conducted multiple analyses to address potential bias from the nurse interventions. Results were reviewed favorably by the FDA. While these analyses demonstrated the consistency of benefit from the CardioMEMS device, all such analyses have methodologic limitations. Early safety data have been suggestive of a higher rate of procedural complications, particularly related to pulmonary artery injury. While the U.S. CardioMEMS post-approval study and CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF) study reported a significant decrease in heart-failure related hospitalizations with few device- or system-related complications at 1 year, the impact of nursing interventions remains unclear. Complete 2-year safety outcomes from the CardioMEMS post-approval study are pending, and the serious adverse event rate in the MEMS-HF trial was 8.9%. Given that the intervention is invasive and intended to be used for a highly prevalent condition, in the light of limited safety data, lack of demonstrable mortality benefit, and pending questions related to its benefit in reducing hospitalizations, the net benefit remains uncertain. Concerns may be clarified by the ongoing GUIDE-HF RCT that proposes to enroll 3600 patients. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring with inert gas rebreathing, no studies were identified that determined how the use of inert gas rebreathing measurements is associated with changes in patient management or evaluated the effects of this technology on patient outcomes. It is unclear how such devices will improve patient outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring of arterial pressure during the Valsalva maneuver, a single study was identified. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. The study assessed the use of LVEDP monitoring and reported an 85% sensitivity and an 80% specificity to detect LVEDP greater than 15 mm Hg. No studies were identified that determined how the use of noninvasive LVEDP estimation is associated with changes in patient management or evaluated the effects on patient outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American College of Cardiology, the American Heart Association, and the Heart Failure Society of America

In 2017, the American College of Cardiology, the American Heart Association, and the Heart Failure Society of America issued joint guidelines on the management of heart failure that offered no recommendations for the use of ambulatory monitoring devices.

Heart Failure Society of America Scientific Statements Committee

In 2018, the Heart Failure Society of America Scientific Statements Committee published a white paper consensus statement on remote monitoring of patients with heart failure and the committee concluded that: "Based on available evidence, routine use of external RPM devices is not recommended. Implanted devices that monitor pulmonary arterial pressure and/or other parameters may be beneficial in selected patients or when used in structured programs, but the value of these devices in routine care requires further study."

National Institute for Health and Care Excellence

In 2018, the National Institute for Health and Care Excellence (NICE) updated their guidelines on chronic heart failure management and did not include outpatient hemodynamic monitoring as a recommendation.

In 2013, the Institute issued guidance on the insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure. The recommendations concluded that "Current evidence on the safety and efficacy of the insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure is limited in both quality and quantity."

Regulatory Status

Computerized Pulse Waveform Analysis

CVProfilor® DO-2020 CardioVascular Profiling System (Hypertension Diagnostics, Inc.) was FDA approved November 1, 2000.

SphygmoCor® Cardiovascular Management System (CvMS) (AtCor Medical Pty. Ltd) was FDA approved August 31, 2007.

Noninvasive Left Ventricular End-Diastolic Pressure Measurement Devices

In 2004, the VeriCor® (CVP Diagnostics), a noninvasive left ventricular end-diastolic pressure measurement device, was cleared for marketing by U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA determined that this device was substantially equivalent to existing devices for the following indication:

"The VeriCor is indicated for use in estimating non-invasively, left ventricular end-diastolic pressure (LVEDP). This estimate, when used along with clinical signs and symptoms and other patient test results, including weights on a daily basis, can aid the

clinician in the selection of further diagnostic tests in the process of reaching a diagnosis and formulating a therapeutic plan when abnormalities of intravascular volume are suspected. The device has been clinically validated in males only. Use of the device in females has not been investigated."

Inert Gas Breathing Devices
In 2006, the Innocor® (Innovision), an inert gas rebreathing device, was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing inert gas rebreathing devices for use in computing blood flow.

Implantable Pulmonary Artery Pressure Sensor Devices
In 2014, the CardioMEMS™ Champion Heart Failure Monitoring System (CardioMEMS, now Abbott) was approved for marketing by the FDA through the premarket approval process. This device consists of an implantable pulmonary artery (PA) sensor, which is implanted in the distal PA, a transvenous delivery system, and an electronic sensor that processes signals from the implantable PA sensor and transmits PA pressure measurements to a secure database.[3,] The device originally underwent FDA review in 2011, at which point FDA found no reasonable assurance that the monitoring system would be effective, particularly in certain subpopulations, although the FDA agreed this monitoring system was safe for use in the indicated patient population.[4,]

Several other devices that monitor cardiac output by measuring pressure changes in the PA or right ventricular outflow tract have been investigated in the research setting but have not received the FDA approval. They include the Chronicle® implantable continuous hemodynamic monitoring device (Medtronic), which includes a sensor implanted in the right ventricular outflow tract, and the ImPressure® device (Remon Medical Technologies), which includes a sensor implanted in the PA.

PRIOR APPROVAL

Not Required.

POLICY

Note: *This policy only addresses the use of these technologies in ambulatory care and outpatient settings.*

See Related Medical Policy

- 02.02.17 Cardiac Contractility Modulation Therapy
- 02.02.18 Noninvasive Measurement of Cardiac Bioimpedance in the Outpatient Setting
- 02.02.19 Baroflex Stimulation Devices
- 02.02.21 Cardiac Hemodynamic Monitoring for the Management of Heart Failure in the Outpatient Setting

- 02.02.22 Non-invasive Heart Failure and Arrythmia Management and Monitoring System

In the ambulatory care and outpatient setting, cardiac hemodynamic monitoring for the management of heart failure using one of the following is considered **investigational,** because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome:

- Implantable direct pressure monitoring of the pulmonary artery CardioMEMS™ Champion Heart Failure Monitoring System (CardioMEMS, now Abbott)
- Inert gas rebreathing (Innocor® [Innovision])
- Left ventricular end-diastolic pressure measurement devices arterial pressure VeriCor® (CVP Diagnostics)

Computerized pulse waveform analysis including but not limited to CV Profilor and SphygmoCor to provide an indication of arterial compliance in the diagnosis and management of cardiovascular events and heart failure is considered **investigational**, because the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 33289 Transcatheter implantation of wireless pulmonary artery pressure sensor for long-term hemodynamic monitoring, including deployment and calibration of the sensor, right catheterization, and pulmonary artery angiography, when performed
- 93050 Arterial pressure waveform analysis for assessment of central arterial pressures, includes obtaining waveform(s), digitization, and application of nonlinear mathematical transformations to determine central arterial pressures and augmentation index, with interpretation and report, upper extremity artery, non-invasive (CV Profilor and SphygmoCor)
- 93264 Remote monitoring of a wireless pulmonary artery pressure sensor for up to 30 days, including at least weekly downloads of pulmonary artery pressure recordings, interpretations(s), trend analysis, and report(s) by a physician or other qualified health care professional (CardioMEMS)
  93799 Unlisted cardiovascular service or procedure (When be utilized for inert gas rebreathing (Innocor® [Innovision])
- C2624 Implantable wireless pulmonary artery pressure sensor with delivery catheter, including all system components

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POLICY HISTORY		
Date	**Reason**	**Action**
January 2022	Annual Review	Policy Revised, New Medical Policy Created

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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