



Cigna Medical Coverage Policy

Subject Thoracic Electrical Bioimpedance for the Measurement of Cardiac Output

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Table of Contents

Coverage Policy	1
General Background	1
Coding/Billing Information	11
References	11

Hyperlink to Related Coverage Policies

[Inert Gas Rebreathing for Cardiac Output Measurement](#)
[Plasma Brain Natriuretic Peptide in the Outpatient Setting](#)

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Coverage Policy

Cigna does not cover thoracic electrical bioimpedance for any indication including the measurement of cardiac output because it is considered experimental, investigational or unproven.

General Background

Cardiac output is a functional measure defined as the volume of blood pumped by the left ventricle in one minute. There is no totally accurate method of measuring cardiac output, but it can be estimated on the basis of various assumptions. The gold standard for measuring cardiac output is use of a thermodilution (TD) catheter. The TD method requires placement of a catheter in the pulmonary artery. When a cardiac output measurement is needed, a small amount of cold saline solution is injected through the catheter. A thermal probe at the catheter tip measures changes in blood temperature following the injection of the cold saline. As the heart pumps warm blood in and cold saline out (thermodilution), the temperature measured by the probe rises back to baseline levels. The area under the TD curve is proportional to cardiac output. Since this is an invasive technique it poses a risk to the patient. Thoracic electrical bioimpedance has been proposed as a noninvasive means of measuring cardiac output and other functional parameters (ECRI, 2012).

Electrical bioimpedance (also referred to as thoracic electrical bioimpedance [TEB], transthoracic bioimpedance, plethysmography, impedance cardiography [ICG], or bioimpedance cardiography) has been investigated as a noninvasive means of providing continuous assessment of cardiac output and other hemodynamic parameters. A small electric current is applied to the chest through electrodes placed on the neck and sides of the chest. Resistance to the current (impedance) is measured through sensors also placed on the neck and sides of the

chest. The pulsatile flow of blood causes fluctuations in the current, and the device calculates cardiac output from the impedance waveform. Electrical bioimpedance has been investigated in a number of different clinical settings, including hospital; ambulatory; and specialty care and for a variety of purposes including diagnosis, assessment, prognosis determination, and management (ECRI, 2012; Albert, 2006).

The use of TEB has been proposed for multiple clinical purposes. These have included differentiation of cardiogenic from pulmonary causes of dyspnea, optimization of atrioventricular (AV) delay, determination of need for inotropic therapy, response to cardiac medications, identification of rejection in patients after heart transplantation, management of fluid and hemodynamics in cardiac patients, evaluate for hypotension in dialysis patients, measuring normal hemodynamic changes during pregnancy and postpartum, assessing fluid retention after major thoracic surgery and management of hypertension (San-Frutos, et al., 2011; Cagini, et al., 2011; Bayya, et al., 2011; Tonelli, et al., 2011; Wang, et al., 2006). However, there is a lack of controlled studies in the published medical literature that validate clinical applications of thoracic bioimpedance or provide comparisons to other noninvasive cardiac diagnostic techniques, such as echocardiography.

Definitive patient selection criteria for TEB have not been established due to conflicting evidence regarding the impact of cardiac output monitoring on patient management and clinical outcomes. Numerous factors may interfere with the accuracy of electrical bioimpedance measurements, including: acute lung injury; significant pulmonary edema; pleural effusion; hemothorax; chest tubes parallel to the aorta; extensive chest wall edema due to crystalloid infusions; dilatation of the aorta; severe mitral regurgitation; severe aortic regurgitation; complete bundle block during cardiopulmonary bypass; presence of a minute ventilation sensor function pacemaker; post-kidney transplant or radical cystectomy; or inability to place electrodes properly. Electrical bioimpedance measurement may also be inaccurate if the patient is moving, agitated, restless, shivering, or hyperventilating (Summers, et al., 2003).

Textbook literature states, "Vascular impedance measurements account for blood viscosity, pulsatile flow, reflected waves, and arterial compliance. Hence, vascular impedance has the potential to describe the dynamic relation between pressure and flow more comprehensively than would be possible using the simpler calculations of vascular resistance. However, because the simultaneous pressure and flow data required for the calculation of impedance are complex and difficult to obtain, the concept of impedance has failed to gain widespread acceptance, and vascular impedance has not been adopted as a routine clinical index" (Davidson, et al., 2011).

U.S. Food and Drug Administration (FDA)

A number of electrical bioimpedance devices have been approved through the 510(k) process of the U.S. Food and Drug Administration (FDA) as Class II devices for the noninvasive monitoring of cardiac output and other hemodynamic parameters. The predicate devices upon which clearance was based are previous cardiac output monitors employing impedance plethysmography. The FDA does not necessarily require clinical data or outcome studies in making a determination of substantial equivalency for the purpose of device approval under section 510(k). There are several FDA-approved devices including, but not limited to: IQ system[®] Cardiac Output Monitor (Renaissance Technologies Inc., Newtown, PA); BoMed[®] NCCOM3-R7 (BoMed Medical Manufacturing, Ltd., Irvine, CA); Hotman System and TEBCO[™] OEM Module (Hemo Sapiens, Inc., Irvine, CA); BioZ[®] (Models BZ-100, 101, and 102), BioZ Portable (Model BZ-125), BioZ[®].com (Model 4110), BioZ.PC (Models BZ 500 and 501) and BioZDX (Model 5100) (SonoSite, Bothell, WA); CIC-1000[™] and Steorra[™] (Sorba Medical Systems, Inc., Brookfield, WI); ICG Module (General Electric Medical Systems Information Technology, Milwaukee, WI) and PhysioFlow[®] Enduro (Vasocom, Inc., Bristol, PA).

Literature Review

Heart Failure (HF): The role of electrical bioimpedance in the evaluation of patients with acute heart failure syndromes is still under investigation. The utility of electrical bioimpedance in the acute management of patients with heart failure will depend on its sensitivity to changes in filling pressures (Nohria, et al., 2005). There is limited evidence supporting the theory that impedance cardiography (ICG) adds to clinical assessment or brain natriuretic peptide (BNP) in predicting poor outcome in heart failure patients (Wang, et al., 2006).

Malfatto et al. (2012) evaluated the reliability of echocardiography, brain natriuretic peptide (BNP), and thoracic electrical bioimpedance (TEB) in predicting pulmonary capillary wedge pressure (PCWP) in 29 patients (72±4 years, New York Heart Association class 3.5±0.9, ejection fraction 28%±6%) who underwent hemodynamic evaluation for worsening HF. Echocardiography was performed immediately before the hemodynamic study. During clinical stability, PCWP, plasma BNP, and TEB were simultaneously assessed. Among TEB variables,

thoracic conductance (thoracic fluid content [TFC]=1/k Ω) was used. For detection of PCWP \geq 15 mm Hg, TFC \geq 35/k Ω had high specificity (97%) and sensitivity (86%) and negative (92%) and positive (97%) predictive value, while E/E' and BNP levels had poorer specificity. After infusion of the inodilator levosimendan, changes in TFC and PCWP were of the same order of magnitude and mutually related. The study did not provide data on the clinical impact on patient management or improved health outcome. The authors reported limitations of this study are the small number of patients included, and the single-center origin of data.

Kamath et al. (2009) studied the utility of ICG in patients hospitalized with heart failure. The BioImpedance CardioGraphy in Advanced Heart Failure study was a prospective substudy of the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness. A total of 170 subjects underwent blinded ICG measurements using BioZ; of these, 82 underwent right heart catheterization. ICG was compared with invasively measured hemodynamics by simple correlation and compared overall ICG hemodynamic profiles. ICG measurements were associated with subsequent death or hospitalization within six months. There was modest correlation between ICG and invasively measured CO (r=0.4–0.6 on serial measurement). Thoracic fluid content measured by ICG was not a reliable measure of pulmonary capillary wedge pressure. There was poor agreement between ICG and invasively measured hemodynamic profiles ($\kappa \leq 0.1$). No ICG variable alone or in combination was associated with outcome. The authors reported that there does not appear to be specific utility for ICG in patients hospitalized with advanced heart failure.

In a cohort study, Castellanos et al. (2009) studied whether the combination of BNP and ICG could be used in a nonacute clinical setting to risk stratify and predict HF-related events in stable outpatients. Patients undergoing routine outpatient echocardiography underwent ICG and BNP testing and were followed for one year for HF-related events (emergency department visit or hospitalization due to HF or all-cause death). A total of 524 patients were analyzed, resulting in 57 HF-related events; 16 emergency department visits, 17 hospitalizations, and 24 all-cause deaths. Using Cox regression analyses, BNP and systolic time ratio index (STRI) by ICG proved to be the strongest predictors of future HF-related events. Patients with a BNP >100 pg/ml and STRI >0.45 sec⁻¹ had a significantly lower event-free survival rate than those with a high BNP and low STRI (67% versus 89%, P=0.001). In patients with LV dysfunction only, if both BNP and STRI values were high, the relative risk of a HF-related event increased by 12.5 (95% C.I. 4.2–36.7), when compared with patients with a low BNP and low STRI (P<0.001). A limitation of this study is it was performed at a single hospital with a homogenous population therefore results of the study can not be generalized to the broad population.

In the “PRospective Evaluation of Cardiac Decompensation in Patients with Heart Failure by Impedance Cardiography Test (PREDICT) Multicenter Trial,” researchers studied whether noninvasive thoracic ICG parameters could predict short-term risk, defined as all-cause death or emergency department (ED) visit or hospitalization due to worsening heart failure. Data were collected every two weeks for 26 weeks in 212 patients. A total of 29% of all patients had events. Multivariate analysis identified six clinical and ICG variables that independently predicted an event within 14 days of assessment. The clinical variables included visual analog score, New York Heart Association functional class, and systolic BP. The ICG parameters included velocity index, thoracic fluid content index, and left ventricular ejection time. The three ICG parameters combined into a composite score were a powerful predictor of an event during the next 14 days. The visits with a high-risk composite score had a 2.5 times greater likelihood, and those with a low-risk score had a 70% lower chance of a near-term event compared with visits at intermediate risk. The researchers caution that their findings are not to be used to titrate therapeutic agents or monitor their effectiveness. It is still not clear whether impedance cardiography-directed modifications improve clinical outcomes beyond that expected if physicians responded appropriately to clinical signals in the absence of ICG data. The clinical importance of these findings is currently being tested in a large-scale trial (Packer, et al., 2006).

In a comparative study, Leslie et al. (2004) evaluated the techniques of thoracic bioimpedance and thermodilution for the measurement of cardiac output in eleven patients with stable chronic heart failure. A total of 282 paired measurements were evaluated. The authors reported that although there was a correlation between thoracic bioimpedance and thermodilution, there was no difference in between-day repeatability between thermodilution and thoracic bioimpedance. Thoracic bioimpedance underestimated cardiac output compared to thermodilution, and this was greater with higher cardiac outputs. The authors reported that their findings suggest that thoracic bioimpedance is not comparable to thermodilution in patients with stable heart failure.

Hypertension: There is limited evidence in the peer-reviewed literature to suggest that determination of hemodynamic parameters by ICG may improve blood pressure (BP) control in patients with hypertension. The studies do not address the long-term patient health outcomes with ICG monitoring. Additional studies are needed to indicate that it is the ICG determinations and not the differences in patients or the treatment algorithm that lead to lower BP (Wang, et al., 2006).

In a randomized, prospective, controlled trial (n=128), Krzesinski et al. (2012) studied the effectiveness of antihypertensive therapy based on hemodynamic assessment by impedance cardiography in patients with arterial hypertension. Patients were randomized into empiric or hemodynamic groups in which treatment choice considered impedance cardiography results. Evaluation of treatment effects was performed after 12 weeks and included office blood pressure measurement and ambulatory blood pressure monitoring. The authors reported that all final blood pressure values were lower in the hemodynamic group, significantly for office systolic blood pressure (empiric versus hemodynamic: 136.1 versus 131.6 mmHg; p=0.036) and diastolic blood pressure (87.0 versus 83.7 mmHg; p=0.013), as well as night-time systolic blood pressure (121.3 versus 117.2 mmHg; p=0.023) and diastolic blood pressure (71.9 versus 68.4 mmHg; p=0.007). Therapy based on impedance cardiography significantly increased the reduction in office systolic blood pressure (11.0 versus 17.3 mmHg; p=0.008) and diastolic blood pressure (7.7 versus 12.2 mmHg; p=0.0008); as well as 24-hour mean systolic blood pressure (9.8 versus 14.2 mmHg; p=0.026), daytime systolic blood pressure (10.5 versus 14.8 mmHg; p=0.040), and night-time systolic blood pressure (7.7 versus 12.2 mmHg; p=0.032). The reported limitation of this study is the lack of long-term patient health outcomes of ICG monitoring. Additionally, the obtained results should be applied with caution in women and in patients with significant chronic diseases since both groups were minorities in this study.

In a randomized controlled trial, the investigators for the Consideration of Noninvasive Hemodynamic Monitoring to Target Reduction of Blood Pressure Levels (CONTROL) study group (Smith, et al., 2006), studied whether ICG-guided treatment could aid physicians in reducing BP more effectively than standard care in a population of uncontrolled hypertensive patients receiving 1–3 medications in a primary care setting. Between November 2002 and November 2004, eleven primary care centers screened 262 patients with a diagnosis of essential hypertension, ages 18–75, on 1–3 antihypertensive medications with systolic BP 140–179 millimeters of mercury (mm Hg) and/or diastolic BP 90–109 mm Hg. Exclusion criteria were: greater than three antihypertensive medications, history of heart failure, ejection fraction < 40%, atrial fibrillation, severe valvular or renal disease, nephrotic syndrome, cirrhosis, and a cerebrovascular event within three months. Patients were also excluded if they had abnormal laboratory findings that are not further described, nor were any laboratory values reported in the study. Technical limitations of ICG also caused exclusion for height < 47 or > 75 inches, weight < 66 or > 341 pounds, hypersensitivity to sensor gel or adhesive, skin lesion at a sensor site, or the presence of activated minute-ventilation pacemaker.

One-hundred eighty-four patients were randomized in a 3:2 ratio to either standard care or ICG-guided care. After randomization, 18 patients were excluded for BP < 140/90 mm Hg upon remeasurement, and two patients withdrew early from the study. No information was provided about the method of randomization. The authors did not indicate the number of patients lost in each study arm. Each of the 164 analyzable patients in the study (95 in the standard arm and 69 in the hemodynamic arm) had a total of five study visits during which BP and ICG measurements were made. Following a baseline visit, they underwent a two-week washout period during which all antihypertensive medications were discontinued. They received a post-washout visit at which physicians prescribed medications consistent with published guidelines, their usual practice patterns, and patient clinical characteristics. This was followed by three monthly visits at which BP was measured and ICG data were obtained on all patients, but ICG findings were not revealed in the standard arm to treating physicians or patients.

In the hemodynamic arm, physicians were encouraged to use, but not required to follow, a hemodynamic treatment strategy. Data are not provided on adherence to the strategy or differences in outcomes within the hemodynamic group based upon adherence. Patients in both arms were educated about medication compliance and received a follow-up phone call from a nurse between visits. ICG data were discussed with the patient by the treating physician in the hemodynamic arm only. Patients were asked how many of their prescribed pills they had taken at each visit as an estimate of compliance. The authors reported very high compliance overall, including 100% of pills taken in both arms of the trial at the fifth visit. Pill count audits were not done.

Information was not provided regarding how long a patient had been under treatment for hypertension prior to study entry. A large percentage of both groups (42% of standard care group and 45% of hemodynamic care group) were on only one antihypertensive medication at baseline. At baseline, standard care patients' BP (in mm Hg.) was $147 \pm 9/87 \pm 10$ and hemodynamic care patients' BP was $148 \pm 12/89 \pm 8$. After washout, standard care BP was $156 \pm 13/92 \pm 9$ and hemodynamic care was $155 \pm 13/94 \pm 9$. The final BP for patients in the standard care group was $136 \pm 15/82 \pm 10$, and for the hemodynamic care group the final BP was $129 \pm 14/76 \pm 11$ ($p < 0.01$). There were no statistically significant differences reported in any hemodynamic measures between the groups at baseline or after washout. The authors reported generalized information as to how hemodynamic data was used. Specific information as to how a particular hemodynamic measurement was used to change patient treatment was not provided. For example, "In the hemodynamic arm, the initial selection of antihypertensive medications appears to have been influenced by the hemodynamic data, because these patients were more likely to be prescribed a vasodilating agent to reduce systemic vascular resistance (SVR) index," and "the hemodynamic treatment strategy influenced medication use when SVR index was considered high, because patients in the hemodynamic arm were more likely to have received an angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blocker (ARB), or calcium channel blocker (CCB), as was suggested."

The authors stated, "In theory, the larger drop in SVR index and BP levels in the hemodynamic arm could have occurred through use of more medications, more effective medications, greater dosing intensity, more effective combination therapy, or better patient compliance. Our study allowed full discretion by the physician in choosing the agents, and a multitude of classes and doses within classes were used." They further stated the study "was designed to determine whether providing hemodynamic data to the physician and the patient could more effectively reduce BP. Whether hemodynamic data led to a more tailored approach to selection and monitoring of antihypertensive agents or by other factors, it resulted in greater reduction in BP and SVR index and better BP control." This study does not address the long-term patient health outcomes of ICG use in uncontrolled hypertensive patients.

In a retrospective case series study, Abelhammed et al. (2005) evaluated nineteen nonhypertensive and 136 hypertensive patients using ICG. Patients were receiving therapy at the time of their evaluation, and medications were not stopped before hemodynamic assessment. The specific dose and agent of hypertensive medication that was added was not noted in this study. There was a limit to the number of normotensive subjects in this study, which limits the statistical power between the groups. Serial hemodynamic assessments were not performed and therefore did not assess the ability of the various ICG variables to characterize changes over time due to disease progression or therapy.

In a retrospective case series study, Sharman et al. (2004) studied ICG-guided decision-making in previously uncontrolled hypertension on two antihypertensive agents in a community generalist setting. The patient inclusion criteria included systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg. All subjects were treated utilizing a previously published ICG-guided treatment algorithm. Twenty-one subjects met the BP and medication criteria. BP at entry was $157.2 \pm 13.9/78.7 \pm 9.9$ mm Hg. Subjects were treated for 215 ± 85 days (5.0 ± 2.0 visits). After ICG-guided treatment, 12/21 (57.1%) achieved sustained BP control ($p < 0.001$). BP was lowered to 141.6 ± 22.0 ($p < 0.001$)/ 77.1 ± 10.7 ($p > 0.05$) mm Hg. Antihypertensive agents increased from 2.0 ± 0.0 to 2.5 ± 0.7 ($p < 0.05$). Diuretics were not widely prescribed in this group of subjects. The authors reported that "Only three (14%) of 21 subjects received an additional diuretic agent during the study period. This was due to patient and physician preference with an appreciation of increased symptoms, and patient noncompliance is often associated with diuretics. While the addition or intensification of diuretics would be a reasonable strategy toward further BP reduction in the uncontrolled group, BP control was achieved in a majority of these subjects without additional diuretic agents." Furthermore, the authors stated, "The fundamental question to be asked in the evaluation of a new information-providing technology for use in clinical management is simply whether the treating physician is more effective with the information than without it."

In a randomized controlled trial, Taler et al. (2002) compared the utility of serial noninvasive hemodynamic measurements by thoracic bioimpedance coupled with a treatment algorithm, to clinical expertise in the selection and titration of antihypertensive therapy for patients with drug-resistant hypertension. Refractory hypertension was defined as BP $> 140/90$ mm Hg while on ≥ 2 antihypertensive medications. This was a three-month treatment program that initially included 117 patients. Patients participating in the study were assigned randomly to treatment based on serial hemodynamic measurements by TEB and a predefined algorithm of medication changes used by the lead investigator who is a hypertension specialist, or to treatment

guided by a hypertension specialist without either TEB or a predefined treatment plan. Patients could be seen by one of several specialists, but the exact number of specialists who participated in the study was not reported. Hemodynamic measurements were obtained for participants in both arms of the study upon entry. However, the data was stored for the specialist care group, and the hemodynamic measurements were not repeated for these patients until the end of the study. All patients in both arms of the study were seen for BP measurements at least monthly. A listing of patient data shows that patients in both arms of the study were seen by the nurse taking BP measurements a mean of 6.2 times during the 90-day study period, or roughly every two weeks. Patients in the hemodynamic-guided treatment arm also received monthly TEB measurements.

Medications for patients in the hemodynamic-guided treatment group were chosen according to the drug algorithm, but details of the treatment algorithm for medication use (e.g., dosages) for patients in the TEB arm are not presented. Also, the study does not provide values for the cardiac index, systemic vascular resistance (SVR) index, or change in thoracic fluid impedance upon which treatment decisions were based. For each of three potential hemodynamic profiles suggested by TEB data, several classes of drugs were available for use requiring clinical judgment by the practitioner in choosing specific medications and doses. Using the treatment algorithm in addition to TEB introduced a second variable into the experimental group, as opposed to the specialist treatment group that used neither. The authors summarized the care of the hemodynamic-guided group as follows: "If cardiac output was less than normal and/or SVR higher than normal, an agent with vasodilatory properties was added or the dosage was increased. Agents that reduce cardiac output were reduced in dosage or discontinued. Alternatively, if cardiac output was above normal and/or SVR was below normal, a beta blocker or central sympathetic agonist was added or increased in dosage, or vasodilatory agents were reduced in dosage or withdrawn. In all cases, attention was addressed to impedance change with posture. Reduced change in impedance with posture (<3 ohms) in association with an elevated BP was interpreted to suggest excess cardiopulmonary volume. In such instances, the diuretic dosage was increased, a more potent diuretic was prescribed, or a second diuretic was started."

Thirteen patients were excluded from the study for various reasons, leaving data on 104 patients for analysis. At the end of the study, mean systolic BP in the hemodynamic-guided treatment group was reduced from 169 to 139 ± 2 ; in the specialist care group, it was reduced from 173 to 147 ± 2 ; and the mean diastolic BP was reduced from 87 to 72 ± 1 and from 91 to 79 ± 1 for each group, respectively. Although patients enrolled in this study had resistant hypertension, both groups experienced large reductions in BP in this short-term study, whether or not TEB was used. The difference in reduction in BP between the groups, however, was statistically significant ($p < 0.01$). The hemodynamic-guided group, which began the study with a mean systolic BP 4 mm Hg lower than the specialist care group, achieved a 30 mm Hg decrease compared to a 26 mm Hg decrease for the specialist care group. Twenty-eight of 50 (56%) patients in the hemodynamic-guided group and 18 of 54 (33%) patients in the specialist care group achieved BPs of $\leq 140/90$ ($p < 0.05$). Medication changes were frequent for patients in both arms of the study, with the hemodynamic group undergoing 5.8 ± 0.4 changes and the specialist group undergoing 4.6 ± 0.5 changes. The most significant change was a near doubling of diuretic dosing in the hemodynamic group from 1.1 ± 0.1 doses per day to 2.1 ± 0.2 doses per day using dosage equivalents developed by the World Health Organization. This is in contrast to diuretic doses in the specialist group that virtually were unchanged, going from 1.2 ± 0.2 to 1.4 ± 0.1 . Actual numbers for the cardiac index and SVR index are not reported in the study. The authors stated that "mean cardiac index did not change during the trial for either group. At entry, SVR was elevated above normal levels in both groups. Intensive drug treatment reduced SVR, with greater incremental reduction in the hemodynamic group."

The authors stated that "targeted control of volume using diuretic therapy achieved BP control superior to that attained by empiric selection of drugs." As evidence that a change in fluid volume was responsible for the change in BP in study participants, volume indicators obtained by TEB measurement are presented. Thoracic fluid impedance measured in ohms was recorded for all participants, both supine and standing, upon entrance into the study and at its conclusion. While the authors stated that "low absolute impedance values and diminished impedance change with posture at entry indicated expanded cardiopulmonary volume in our patients," the authors do not indicate what a normal fluid volume would be, or how many patients were able to achieve it. The authors stated that "impedance levels rose with more intensive diuretic dosage in both treatment groups suggesting a reduction in cardiopulmonary volume, although we did not see an incremental rise with the higher doses used in the hemodynamic group." The authors stated that "improved BP control correlated with an incremental reduction in systemic vascular resistance (SVR) in those treated according to hemodynamic values." The values were presented in graph format only without the actual numbers. The authors reported that

there were more changes in medication choices and treatment intensity in the hemodynamic care group. This study does not address the long-term patient health outcomes of ICG monitoring.

Yung et al. (2004) compared the accuracy of ICG to that of TD and direct Fick in the measurement of cardiac output and cardiac index in pulmonary-artery hypertension patients. The study analyzed 39 enrolled patients: 44% male, average age 50.8 years. Results comparing ICG to pulmonary artery catheter (PAC) were as follows: ICG versus Fick (-0.13 L/min/m² and 0.46 L/min/m²), thermodilution (TD) versus Fick (0.10 L/min/m² and 0.41 L/min/m²), ICG versus TD (respectively with 95% level of agreement between -0.72 and 0.92 L/min/m²; cardiac output correlation of ICG versus Fick, TD versus Fick and ICG versus TD was 0.84, 0.89, and 0.80, respectively. This study suggests that ICG may provide an accurate method for determining cardiac output in pulmonary hypertension patients and serve as a tool for following responses to therapeutic interventions.

Dyspnea: Limited evidence is available that evaluates the clinical impact on patient management and/or improved health outcomes from the use of electrical bioimpedance monitoring for differentiation of cardiogenic from pulmonary causes of acute dyspnea. Well-designed controlled studies are needed to establish the value of ICG in assessing patients with dyspnea.

In a prospective study, Lo et al. (2007) compared ICG results in differentiating cardiac from noncardiac causes of dyspnea to ED physician diagnoses. A total of 52 patients were included in the study. Compared with the final diagnoses, the overall diagnostic accuracy for ED physicians was 69% (36/52) versus 83% (43/52) for ICG. ED physicians diagnosed 13 of 20 patients correctly with a final diagnosis of cardiac-caused dyspnea, and 23 of 32 for noncardiac-caused dyspnea. If the ED physician diagnosed both cardiac and noncardiac causes in the same patient, the authors favored diagnosis by ED physicians according to the treatment at the ED. ICG correctly diagnosed 15 of 20 patients with cardiac cause, and 28 of 32 with noncardiac cause. The authors reported that ICG had superior sensitivity (75%/60%), specificity (88%/66%), positive predictive value (79%/52%), and negative predictive value (85%/72%) over ED physicians, respectively, in the final diagnosis of cardiac versus noncardiac causes of dyspnea. The reported limitations of this study include a small sample size and retrospective criteria for ICG diagnosis. The authors stated that a prospective trial is needed to provide greater confidence in which hemodynamic parameters of ICG have the greatest value in assessing patients in the ED.

In a prospective study, Peacock et al. (2006) studied the rate of change in diagnosis and therapy resulting from the availability of ICG data during the initial evaluation of ED patients 65 years of age or older presenting with dyspnea. Eighty-nine patients were enrolled. Congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD) were the most common final diagnoses, occurring in 43 (48%), and 20 (22%), respectively. ICG data changed the working diagnosis in 12 (13%) and medications administered in 35 (39%). The authors reported that it is possible that a physician had the right diagnosis and treatment plan before reviewing ICG results and that ICG data resulted in inappropriate therapies. The authors stated a larger outcomes-based study is needed.

Ischemic Heart Disease: Gujjar et al (2010) compared cardiac output (CO) measured by TEB with that measured by multi-gated radionuclide equilibrium cardiography (RNEC). A total of 32 patients with proven or suspected ischemic heart disease, but without overt cardiac failure, edema or arrhythmias were studied. Reported limitations are that this study was restricted to outpatients with relatively well preserved cardiac functions. Hence the comparison may not be generalized to other clinical situations. Additionally, the percentage error of 42% is moderately higher than an acceptable 30% recommended for such studies comparing physiologic measurements by two different methods. The authors reported that this comparative study found a moderate correlation between TEB and RNEC methods of CO measurement. They stated that further studies are needed to examine the relative utility of TEB in comparison with RNEC as well as other methods of CO measurement before considering its use in patients with ischemic heart disease.

Optimization of AV Delay: Adjustment of AV delay has been proposed as a means of improving cardiac output in patients with dual chamber pacemakers and heart failure. Studies have not identified an optimal AV delay in patients with heart failure. Therefore, it is difficult to know the significance of the reported correlation between echocardiographic and ICG determination measurements of cardiac output. Studies that support the beneficial long-term health outcomes using ICG data have not been performed (Wang, et al., 2006, Jordan, et al., 2002).

In a descriptive study, Heinroth et al. (2007) presented data from the routine use of ICG-based cardiac output measurements to guide the optimization of AV- and interventricular (VV)-interval timing of cardiac

resynchronization therapy (CRT) devices. Forty-six patients with heart failure (left ventricular ejection fraction <35%, New York Heart Association [NYHA] III–IV) and left bundle branch block (>130 milliseconds [ms]) in sinus rhythm were evaluated 3–5 days after implantation of a CRT device by means of ICG. Cardiac output was measured without pacing and with biventricular pacing using a standard protocol of VV- and AV-interval modification from -60 to +60 ms and 80–140 ms, respectively, in 20 ms steps. Mean CO without pacing was 3.66 ± 0.85 L/min and significantly increased to 4.40 ± 1.1 L/min ($p < 0.05$) with simultaneous biventricular pacing and an AV interval of 120 ms. ‘Optimizing’ both VV and AV intervals further increased cardiac output to 4.86 ± 1.1 L/min ($p < 0.05$). Maximum cardiac output was measured in most patients with left ventricular pre-excitation. The proportion of nonresponders to CRT was reduced by 56% following AV- and VV-interval modification using ICG guidance. The authors reported that further work is needed to determine the utility of ICG-derived data in combining AV and VV intervals to ideally suit any given patient.

Braun et al. (2005) evaluated the ability of ICG to measure changes in cardiac output caused by different AV intervals in patients with CRT and to compare these data with transaortic DE to optimize the AV interval during biventricular pacing. The study population consisted of 24 patients with a left ventricular ejection fraction <35%, left bundle branch block (QRS duration >150 ms), and sinus rhythm who had received a cardioverter defibrillator with biventricular pacing for CRT (CRT-D). All patients were in stable NYHA Class III–IV after receiving an optimal medical therapy for ≥ 1 month. The optimal AV interval was defined by ICG and subsequently by transaortic flow DE as the interval corresponding to the highest cardiac output measured at different AV intervals, varying from 60–200 ms (with 20 ms increments). For standardization and comparison of both techniques, a fixed atrioventricular pacing rate of 90 beats/min was used. Absolute values of cardiac output maximum were higher by ICG (5.8 ± 0.9 l/min) as compared to DE (4.6 ± 0.9 l/min, $p < 0.01$). The optimal AV interval as determined by ICG varied interindividually from 80–180 ms (mean: 121 ± 18 ms). In DE, the range was also 80–180 ms with the mean optimal AV interval of 128 ± 23 ms. Thus, there was a strong correlation for AV-interval optimization in CRT between both methods ($r = 0.74$; $p < 0.001$). The authors reported that in CRT, AV-interval optimization based on cardiac output values determined by IC correlates closely to those measured by transaortic flow DE. A reported limitation of this study is that the results on the optimal AV-interval vary interindividually. Therefore, the absolute mean value is not easily applicable for routine use in a particular patient, and a separate investigation needs to be performed in each patient.

Rejection in Patients after Heart Transplantation: ICG in conjunction with endomyocardial biopsy for detection of rejection in patients after heart transplantation has been proposed. Preliminary findings in a case series study of 35 patients (Weinhold, et al., 1993) with heart transplants reported that a decrease in acceleration index was 71% sensitive and 100% specific for rejection. The study did not provide data on the clinical impact on patient management or improved health outcome after treatment. No other study has confirmed these preliminary findings (Wang, et al., 2006; Jordan, et al., 2002).

Other Conditions: In a prospective study, Van DeWater et al. (2003) compared the accuracy of ICG to TD via PAC in postoperative coronary artery bypass graft (CABG) patients. This study took place in a cardiovascular-thoracic surgery intensive care unit (ICU). The study included 53 post-CABG patients from whom 210 pairs of cardiac output measurements were made. The ICG cardiac output was determined simultaneously with the TD cardiac output. The authors reported that when comparing ICG to TD, they found that the bias, precision, correlation slope, and intercept were equivalent to TD. The authors stated that in those circumstances in which intracardiac pressures and mixed venous blood samples are not necessary, ICG is preferable to TD via PAC in determining cardiac output. The authors stated that the ICG monitor allows for quick and easy cardiac output monitoring and systemic vascular resistance (SVR) in clinical areas where the PAC is not typically utilized (e.g., emergency department, subacute care, and outpatient hypertension and heart failure clinics). The authors reported that the advancements with the BioZ ICG monitor with ZMARC equation allowed equivalence to TD that was not found with the older ICG monitors and equations.

Sageman et al. (2002) prospectively compared two types of cardiac output measurement in patients after cardiopulmonary bypass: TEB cardiography and pulmonary artery thermal dilution (TD)-derived cardiac index. Participants included 20 post-cardiopulmonary-bypass patients for primary comparison between technologies and 20 for comparison of variability within each technology. Cardiac index values were collected simultaneously by TEB or TD, and the results were calculated over time. The authors reported that TEB is a promising, noninvasive, potentially low-cost alternative to TD and premature atrial contraction (PAC) hemodynamic measurement in the ICU. Much work remains, however, to prove time-tested clinical utility and patient outcome improvement.

Technology Assessments

The Agency for Healthcare Research and Quality (AHRQ) published a technology assessment of TEB initially in 1992 and in 2002. A systematic review and meta-analysis of the TEB literature from 1991 to July 2002 was performed. The authors concluded, "Due to limitations in the studies, no meaningful conclusions can be drawn about the accuracy of TEB, compared to alternative measures of hemodynamic parameters. There is also little conclusive evidence regarding TEB's usefulness in the specific clinical areas addressed. This was largely due to the lack of focus on clinical outcomes by researchers in this area. The clinical reports on the use of TEB for a variety of clinical indications in reports published from 1991 onwards suggested that this non-invasive method is of interest and may potentially support some of these indications, but there is limited evidence that directly addressed how this monitoring technique can affect patient outcomes." The clinical areas addressed and the AHRQ conclusions include the following (CMS, 2003; Jordan, et al., 2002):

- Known or suspected cardiovascular disease: "No studies provided information on health outcomes, or on patient management, or on clinical end-points to address the usefulness of TEB in monitoring or management."
- Differentiation of cardiogenic from pulmonary causes of acute dyspnea: "No studies were found that evaluated the clinical impact on patient management and/or improved health outcomes from the use of TEB monitoring for differentiation of cardiogenic from pulmonary causes of acute dyspnea."
- Optimization of AV interval with A/V sequential pacemakers: "Some of the evidence suggests that TEB is potentially useful in patients with pacemakers. None of the studies reported health outcomes after adjustment of the A/V delay, so the evidence is insufficient to conclude whether TEB optimization of the A/V delay improves health outcomes."
- Determination of the need for intravenous inotropic therapy: No studies were identified that evaluated the clinical impact on patient management and/or improved health outcomes that would support the use of TEB.
- Post-heart transplant myocardial biopsy: A preliminary study was found that might be useful if replicated but found no subsequent peer-reviewed studies relating TEB to post-heart transplant myocardial biopsy.
- Patients in need of fluid management: No studies were found.
- Hypertension: Only one study reported patient outcomes (Taler, et al., 2002) but the authors reported that the results may not be generalized to community practice.

Raajmaker et al. (1999) performed a meta-analysis of 154 studies published prior to 1997 comparing ICG with thermodilution and indirect Fick. The authors reported that "the overall r^2 value of 0.67 indicates that thoracic ICG might be useful for trend analysis of different groups of patients. However, for diagnostic interpretation, an r^2 value of 0.53 might not meet the required accuracy of the study." The authors stated that "great care should be taken when thoracic ICG is applied to the cardiac patient." The values for cardiac patients were an r^2 of 0.59 and 0.44, in repeated measurement and single measurement designs, respectively.

Centers for Medicare and Medicaid Services (CMS)

In a decision memorandum (2003), the CMS after doing a complete and updated literature review, reconsidered their 1998 decision to cover TEB devices from "noninvasive diagnosis or monitoring of hemodynamics in patients with suspected cardiovascular disease" to numerous clinical indications. CMS made another reconsideration of their policy in 2006, and CMS will continue the current TEB policy for the following indications:

- Differentiation of cardiogenic from pulmonary causes of acute dyspnea when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;
- Optimization of AV interval for patients with an AV sequential pacemaker when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient; and
- Monitoring of continuous inotropic therapy for patients with terminal CHF, when those patients have chosen to die with comfort at home, or in patients waiting at home for a heart transplant;

- Evaluation for rejection in patients with a heart transplant as a predetermined alternative to a myocardial biopsy. Medical necessity would need to be documented should a biopsy be performed after TEB.
- Optimization of fluid management in patients with CHF when physician history, physical examination, and standard assessment tools provide insufficient information, and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;
- CMS determines that the coverage and description of the specifics of the situation in which TEB is reasonable and necessary for the treatment of drug-resistant hypertension is left to carrier discretion. CMS states that additional evidence does not warrant expanding coverage at this time. Drug-resistant hypertension is defined as failure to achieve goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic.

TEB continues to be non-covered when used for monitoring of patients with:

- Proven or suspected disease involving severe regurgitation of the aorta
- Minute ventilation (MV) sensor function pacemakers, since the device may adversely affect the functioning of that type of pacemaker; or
- During cardiac bypass surgery

Due to an absence of evidence, CMS considers all other uses of TEB as noncovered.

Professional Societies/Organizations

The 2013 states that other options for diagnostic evaluation of patients with suspected acutely decompensated heart failure, such as noninvasive cardiac output monitoring are not yet validated (Yancy, et al., 2013).

The ACC commented on the reconsideration of CMS's national coverage determination for electrical bioimpedance for cardiac output (CMS, 2006). The ACC stated, "We found that the evidence does not support establishment of national Medicare coverage as requested for hypertensive patients on one or more anti-hypertensive drugs who are not at goal BP. Our clinical experts noted that the two small randomized studies cited by the requester focused only on patients with BP that was quite difficult to control. The patients were typically on multiple antihypertensive drugs and were, on average obese. These factors limit the extent to which the results of the studies can be generalized to the broader population of patients who have failed to achieve desired BP control on only one or more antihypertensive drugs. The studies cited do provide some evidence of benefit for a more narrowly defined patient population. The ACC states that Medicare coverage for patients with drug resistant hypertension, defined as failure to achieve goal BP when adhering to full doses of an appropriate three drug regimen, including a diuretic may be appropriate."

Use Outside of the US

The 2012 European Society of Cardiology (ESC) guideline for the diagnosis and treatment of acute and chronic heart failure states, "Management adapted in response to monitoring thoracic impedance (as an indirect measure of intrathoracic fluid) has not been shown to improve outcomes. The optimum approach to non-invasive remote monitoring is uncertain, and RCTs performed to date have given inconsistent results and do not yet support a guideline recommendation" (McMurray, et al., 2012).

Summary

Pulmonary artery catheterization is an invasive technique that has been used to obtain cardiac output measurements. Thoracic electrical bioimpedance is one of several noninvasive techniques that have been investigated to measure cardiac output and other hemodynamic parameters.

Opinions in the current literature continue to be conflicting as to the utility of thoracic electrical bioimpedance in measuring cardiac output and other hemodynamic parameters. Although small, often uncontrolled studies in outpatient as well as inpatient populations indicate the feasibility of thoracic electrical bioimpedance, there is insufficient evidence in the published peer-reviewed medical literature to indicate that thoracic electrical bioimpedance for the measurement of cardiac output is comparable to available methods. Additionally, the

patient selection criteria have not been clearly defined, and unanswered questions remain regarding the appropriate role in patient management and health outcomes.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
93701	Bioimpedance-derived physiologic cardiovascular analysis

*Current Procedural Terminology (CPT®) © 2013 American Medical Association: Chicago, IL.

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