Policy Replaced with LCD L34555
Effective February 26, 2018

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Computerized 2-lead Resting Electrocardiogram Analysis for the Diagnosis of Coronary Artery Disease

Policy #459:
Category: Medical

Latest Review Date: July 2017
Policy Grade: Active policy but no longer scheduled for regular literature reviews and updates.

Background:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Description of Procedure or Service:

Computerized 2-lead resting electrocardiogram analysis (e.g., multifunction cardiogram) is a computerized analysis of a 2-lead resting electrocardiogram that has been proposed for use as a diagnostic test for coronary artery disease (CAD).

The 12-lead resting electrocardiogram (ECG) analysis is a standard tool in the detection of acute cardiac ischemia, but has less accuracy for monitoring for chronic changes associated with coronary artery disease (CAD). Therefore, the resting ECG has only a limited role in the diagnosis of chronic CAD. Stress testing, either at rest or with exercise, combined with single-photon emission computed tomography or echocardiographic imaging, is the most common initial test in the diagnostic work-up of chronic CAD. Sensitivities and specificities for stress testing vary but generally fall in the 75% to 90% range. Cardiac angiography is the criterion standard for diagnosing CAD and is used in situations in which CAD needs to be confirmed following stress testing.

The multifunction cardiogram is intended to improve on the performance of the standard ECG for diagnosing CAD. The study device records a 2-lead ECG tracing for 82 seconds using leads II and V5 together with proprietary hardware and software. The analog ECG tracing is then amplified, digitized, down-sampled to a rate of 100Hz, and encrypted for digital transmission. The digitized information is transmitted to a central server for further analysis. At the central server, the tracings undergo a series of mathematical transformations and signal averaging. Six mathematical transformations included: power spectrum, coherence, phase angle shift, impulse response, cross-correlation, and transfer function. Following these transformations, the patterns found in the tracing are compared to a large reference database collected by the manufacturer. A severity score is generated, indicating the likelihood that CAD is present. The severity score ranges from 0-20, with a score of 4.0 suggested as the cutoff for the presence of clinically significant CAD.

Policy:

Effective for dates of service on or after February 26, 2018 refer to LCD L34555

Effective for dates of service on or after January 25, 2011 and prior to February 26, 2018:
Blue Advantage will treat **Computerized 2-lead resting electrocardiogram analysis** (e.g., multifunction cardiogram) for diagnosing coronary artery disease as a **non-covered benefit** and as **investigational.**

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was updated through March 23, 2017.

Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) its technical performance (test-retest reliability or interrater reliability); (2) diagnostic accuracy (sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) clinical utility (i.e., a demonstration that the diagnostic information can be used to improve patient outcomes). The following is a summary of the key literature to date.

Electrocardiogram Analysis for Diagnosis of Coronary Artery Disease

Clinical Context and Proposed Clinical Utility

The proposed clinical utility of computerized 2-lead resting ECG analysis evaluated in this review is to improve the accuracy of CAD screening and to identify those patients who would benefit from coronary artery intervention.

The current standard intervention is a clinical workup which includes physical examination, family history-taking, risk score calculation and stress-testing with or without additional imaging. Standard 12-lead resting ECGs have limited diagnostic accuracy in asymptomatic patients. Thus, an objective test that can improve on the accuracy of the standard clinical workup could be clinically beneficial.

The question addressed in this evidence review is: In individuals being screened for CAD, does use of computerized 2-lead resting ECG analysis improve the identification of patients who would benefit from medical or surgical coronary artery intervention and/or lead to improved health outcomes compared with a standard clinical workup?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is patients being screened for CAD.

Interventions

The intervention is computerized 2-lead resting ECG analysis.

Comparators

The comparator of interest is a standard clinical workup including physical examination, family history-taking, risk score calculation and stress-testing with or without additional imaging.

Outcomes

The primary outcomes of interest are overall survival (i.e., reduction in the rate of sudden cardiac death) and morbid events (e.g., myocardial infarction). Other outcomes of interest are test accuracy and validity.

Timing

Because patients are asymptomatic, longer-term outcome measurement would be appropriate (e.g., assessing morbid events and overall survival after 6 months, 1 year or longer).

Setting
Patients would be tested in the nonacute primary care or specialty care (e.g., cardiology) setting.

Technical Performance
No specific studies of technical performance were identified.

Diagnostic Accuracy
Systematic Reviews
A systematic review and meta-analysis was published by Strobeck et al. This combined analysis included 1076 patients from 44 diagnostic accuracy studies. Hemodynamically significant CAD was diagnosed in 43.4% (467/1076) of patients. The calculated sensitivity and specificity of the multifunction cardiograms were 91.2% and 84.6%, respectively. The positive predictive value (PPV) was 78% and the negative predictive value (NPV) was 94%. The area under the curve (AUC) by receiver operating characteristic (ROC) analysis was 88.1% (95% confidence interval [CI], 86% to 90.3%). Using a severity score of 4.0 as the cutoff for a positive test, the likelihood ratio positive was 5.9, and the likelihood ratio negative was 0.10. There were only minor differences between centers in the sensitivity and specificity; the statistical significance of these differences was not tested.

Diagnostic Accuracy Studies
Grube et al (2007) published the largest study on the accuracy of the multifunction cardiogram for diagnosing CAD. The study population consisted of 562 patients with no prior history of coronary revascularization who were scheduled to receive coronary angiography over a 1-year period at 1 institution in Germany. All patients underwent multifunction cardiogram and coronary angiography, with results of each modality interpreted independently and blinding of the results of the other test(s). A total of 139 (24.7% of total) patients were excluded from analysis; 17 because of poor-quality electrocardiogram (ECG) tracing and 122 because full risk-factor data were not available, leaving 423 patients in the final analysis. Obstructive coronary disease, defined as at least 1 stenosis greater than 70%, was diagnosed in 47.5% of patients (201/423). Multifunction cardiograms in this group had a reported sensitivity of 89.1% and a specificity of 81.1%; the PPV was 79% and the NPV was 90%. The calculated AUC by ROC analysis was 84.3% (95% CI, 80.2% to 88.4%).

Grube et al (2008) published a companion article on 213 patients scheduled for angiography who had previously undergone revascularization. The protocol and analysis for this study was identical to the earlier article, except for the presence or absence of prior revascularization. A total of 41 patients were excluded from analysis, leaving a final sample of 172 patients. In this sample, obstructive coronary disease, defined as at least 1 stenosis greater than 70%, was diagnosed in 32% of patients (55/172). The estimated sensitivity and specificity were 90.9% and 88.0%, respectively. The PPV was 62.7% and the NPV was 97.8%.

Weiss et al (2002) assessed 200 ambulatory patients who were scheduled to undergo coronary angiography at 1 institution in New York. All patients underwent multifunction cardiogram; however, 64 (32% of total) patients had ECG tracings of insufficient quality and were excluded from analysis, leaving 136 patients in the final sample. The authors did not state whether the test

results were interpreted in an independent and blinded manner. Obstructive coronary disease, defined as at least 1 stenosis greater than 70%, was diagnosed in 57.4% (78/136) of patients. The reported sensitivity and specificity of multifunction cardiogram were 93.3% and 83%, respectively. The PPV was 91.2%, and the NPV was 86.7%. The calculated AUC by ROC analysis was not reported.

Hosokawa et al enrolled 222 patients who were scheduled to receive coronary angiography over an approximately 6 month period from 5 medical centers in Asia. All patients underwent multifunction cardiogram and coronary angiography, with results of each modality interpreted independently and blinded to the results of the other test(s). A total of 33 patients (14.9% of total) were excluded from analysis, 3 because of poor-quality ECG tracing and 30 because coronary angiograms were not available for interpretation, leaving 189 patients in the final analysis. Obstructive coronary disease, defined as at least 1 stenosis greater than 60%, was diagnosed in 40.7% of patients (77/189). The reported sensitivity and specificity of multifunction cardiogram were 94.8% and 86.6%, respectively. The PPV was 78.4% and the NPV was 97.1%. The calculated area under the curve was 91.4% (95% CI 86.8 to 96.1%).

The 4 studies described above were included in the systematic review by Strobeck et al. Three additional studies of the diagnostic accuracy of the multifunction cardiogram have been published since that time. In 2011, Strobeck et al compared its accuracy to single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) using angiography as the criterion standard. This study enrolled 165 consecutive patients with known or suspected CAD and/or valvular heart disease who agreed to participate. Of the 165 patients, 49 did not undergo angiography due to a normal SPECT exam and no other indications for angiography; of these, 8% (4/49 patients) had an abnormal computerized 2-lead electrocardiogram. These patients were excluded from further analysis, leaving 116 patients in the study who received all 3 tests (computerized 2-lead resting ECG, SPECT MPI, angiography). The sensitivity and specificity of the computerized 2-lead resting ECG were 91% (95% CI, 79% to 97%) and 87% (95% CI, 76% to 94%), respectively, compared with a sensitivity of 85% (95% CI, 72% to 93%) and a specificity of 14% (95% CI, 7% to 25%) for SPECT MPI. Subgroup analyses revealed similar accuracy by gender, severity of coronary obstruction, and age. The specificity for SPECT MPI in this study was markedly lower than that reported previously. In a recent meta-analysis of 13 studies (total N=1323 subjects), the pooled estimate for specificity of SPECT was 77% (95% CI, 64% to 86%), and the pooled sensitivity was 83% (95% CI, 81% to 91%). The reduced specificity reported in the Strobeck study may have been related to the performance of angiography in patients with valvular disease, because these patients may have had higher rates of false-positive SPECT exams than patients with suspected ischemia.

Two smaller studies of diagnostic accuracy were published in 2014 and 2015. They enrolled 100 and 112 patients, respectively, who were scheduled to undergo coronary angiography. In both, individuals interpreting the computerized 2-lead resting electrocardiogram were independent and blinded to the results of angiography. In 1 study, the reported specificity of computerized 2-lead resting electrocardiogram was high (90.4%; 95% CI, 87.0% to 93.9%), and the sensitivity was lower (48.1%; 95% CI, 38.5% to 57.8%), with an NPV of 82.5% (95% CI, 78.3% to 86.7%). In the other study, the reported specificity (67%) and sensitivity (32%) for functional ischemia were lower, with an NPV of 57%.

Section Summary: Diagnostic Accuracy

There are a number of diagnostic accuracy studies and a 2009 systematic review. The systematic review found a calculated sensitivity and specificity of 91.2% and 84.6%, respectively. However, most published studies have several methodologic limitations that reduce their internal validity. In all but one, the population is a convenience sample of patients who underwent angiography. These patient populations are thus subject to a referral or "work-up" bias in that the population of patients that might be considered for the computerized 2-lead resting electrocardiogram in clinical practice are not the same population being referred for angiography. Also, the number of patients enrolled but not included in the analysis was relatively high, ranging from 14.9% to 32% of the total number of enrollees. These high rates of exclusion raise the potential for biased estimates of test sensitivity and specificity. Finally, in one of the cohorts, angiogram and multifunction cardiogram results were not interpreted in an independent and blinded manner. These methodologic limitations create a substantial degree of uncertainty regarding the reported results for diagnostic accuracy.

Clinical Utility

There were no published articles that directly addressed the clinical utility of a computerized 2-lead resting electrocardiogram. The impact of this technology on patient management decisions is uncertain. While it is possible that the results of this test may influence patient management, for example, the decision to perform angiography, the evidence on this question is incomplete. As a result, clinical utility has not been demonstrated and the impact on health outcomes is unknown.

Section Summary: Clinical Utility

No published studies were identified that demonstrate how computerized 2-lead resting electrocardiogram can be used to change clinical management in ways that improve health outcomes. Moreover, given uncertainties in the diagnostic accuracy of this technology and how it might be incorporated into clinical practice, a chain of evidence demonstrating potential clinical utility is unavailable.

Summary of Evidence

For individuals who are being screened for coronary artery disease (CAD) with computerized 2-lead electrocardiography, the evidence consists of several diagnostic accuracy studies and a systematic review. Relevant outcomes include overall survival, disease-specific, test accuracy, test validity, and morbid events. The systematic review found a calculated sensitivity and specificity of 91.2% and 84.6%, respectively. However, studies included in the systematic review had several methodologic limitations that reduced their internal validity. For example, they used convenience samples and had high rates participants exclusion from the analysis. These methodologic limitations create a substantial degree of uncertainty regarding the reported results for diagnostic accuracy. The clinical utility of the technology is also uncertain. Even if this test has good accuracy for diagnosing CAD, its application in clinical practice would still need to be determined. Use of the computerized 2-lead electrocardiogram analysis to screen for CAD would depart from usual practice, because screening for CAD has not been shown to improve outcomes. In the non-acute setting, the most common method for diagnosing CAD is stress testing, and there is no evidence comparing the accuracy of computerized 2-lead

electrocardiography with stress testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force (USPSTF) recommendations for computerized 2-lead resting electrocardiogram analysis in patients being screened for coronary artery disease have been identified.

Key Words:
Multifunction cardiogram, 3DMP, coronary artery disease, CAD, atherosclerotic heart disease

Approved by Governing Bodies:
There is at least one commercially available multifunction cardiogram. In April 2003, the Premier Heart MCG™ system (Premier Heart, Port Washington, NY) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. FDA determined that this device was substantially equivalent to existing devices for use in ECG analysis

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Current Coding:
CPT codes:

0206T	Computerized database analysis of multiple cycles of digitized cardiac, electrical data from two or more ECG leads, including transmission to a remote center, application of multiple nonlinear mathematical transformations, with coronary artery obstruction severity assessment.

References:

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3. Grube E, Bootsveld A, Buellesfeld L et al. Computerized two-lead resting ECG analysis for the detection of coronary artery stenosis after coronary revascularization. Int J Med Sci 2008; 5(2):50-61.
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7. Strobeck JE, Mangieri A, Rainford N. A paired-comparision of the Multifunction Cardiogram (MCG) and sestamibi SPECT myocardial perfusion imaging (MPI) to quantitative coronary angiography for the detection of relevant coronary artery obstruction (>/=70%) - a single-center study of 116 consecutive patients referred for coronary angiography. Int J Med Sci 2011; 8(8):717-24.
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9. Weiss MB, Narasimhadevara SM, Feng GQ et al. Computer-enhanced frequency-domain and 12-lead electrocardiography accurately detect abnormalities consistent with obstructive and nonobstructive coronary artery disease. Heart Dis 2002; 4(1):2-12.

Policy History:

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Medical Policy Group, June 2012
Medical Policy Group, January 2013
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Medical Policy Group, February 2018