
Medical Policy



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.

***Current Policy Effective Date: 5/1/20**
(See policy history boxes for previous effective dates)

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

Description/Background

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). This policy will review the evidence on accuracy and clinical utility of the multifunction cardiogram.

The standard 12-lead resting electrocardiogram (ECG) has limited diagnostic accuracy in the detection of coronary artery disease (CAD). Because of its limited accuracy, 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 (SPECT) 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 75-90% range. Cardiac angiography is the gold 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 100 Hz, 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. There are 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.

Regulatory Status:

There is at least one commercially available multifunction cardiogram, the 3DMP device, manufactured by Premier Heart MCG™, LLC (Port Washington, NY). In April 2003, the 3DMP device was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA determined that this device was equivalent to existing devices for use in ECG analysis.

Medical Policy Statement

Computerized 2-lead resting electrocardiogram analysis (e.g., multifunction cardiogram) is considered experimental/investigational for diagnosing coronary artery disease. Its use has not been clinically proven to improve patient outcomes.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

89240

Rationale

Articles were retrieved that included primary data on the accuracy, predictive value, or clinical utility of multifunction cardiogram for the diagnosis of coronary artery disease (CAD). The available evidence on the accuracy of multifunction cardiogram consists of several cross-sectional studies that evaluate the performance characteristics of the test in patients with suspected CAD, using coronary angiography as the criterion standard.

ELECTROCARDIOGRAM ANALYSIS FOR DIAGNOSIS OF CORONARY ARTERY DISEASE

Clinical Context and Proposed Clinical Utility

The proposed clinical utility of computerized 2-lead resting electrocardiogram (ECG) analysis evaluated in this review is to improve the accuracy of coronary artery disease (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 a medical or surgical coronary artery intervention and/or lead to improved health outcomes compared with a standard clinical workup?

The following **PICOTS** was used to select literature to inform this review.

Patients

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

Interventions

The intervention of interest 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 (egg, 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.¹ 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 is the largest study on the accuracy of multifunction cardiogram for diagnosing coronary artery disease (CAD).² 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 one institution in Germany. 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 139 (24.7% of total) patients were excluded from analysis, 17 because of poor-quality 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 one stenosis greater than 70%, was diagnosed in 47.5% of patients (201/423). The reported sensitivity and specificity of multifunction cardiogram were 89.1% and 81.1%, respectively. The positive predictive value (PPV) was 79.4%, and the negative predictive value (NPV) was 90.0%. The calculated area under the curve by receiver operating characteristic (ROC) analysis was 84.3% (95% confidence interval [CI]: 80.2-88.4%).

Grube et al published a companion article on 213 patients scheduled for angiography who had previously undergone revascularization.³ The protocol and analysis for this study was identical to the first 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 one stenosis greater than 70%, was diagnosed in 32% of patients (55/172). The estimated sensitivity and specificity were 90.9% and 88.9%, respectively. The PPV was 62.7% and the NPV was 97.8%.

Weiss et al included 200 ambulatory patients who were scheduled to undergo coronary angiography at one institution in New York.⁴ All patients underwent multifunction cardiogram; however, 64 patients (32% of total) had electrocardiogram (ECG) tracings of insufficient quality and were excluded from analysis, leaving 136 patients in the final sample. The authors did not state that the test results were interpreted in an independent and blinded manner. Obstructive coronary disease, defined as at least one stenosis greater than 60%, was diagnosed in 57.4% of patients (78/136). The reported sensitivity and specificity of multifunction cardiogram were 89.1% and 81.1%, respectively. The PPV was 79.4%, and the NPV was 90.0%. The calculated area under the curve 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 five medical centers in Asia.⁵ 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 one 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 by ROC analysis was 91.4% (95% CI: 86.8-96.1%).

The four 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, an additional study of diagnostic accuracy was published by Strobeck et al that compared the accuracy to SPECT MPI (myocardial perfusion imaging) using angiography as the gold standard.⁶ This study enrolled 165 consecutive patients with suspected coronary disease 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 49 patients, 8% (4/49 patients) had an abnormal computerized 2-lead electrocardiogram. The 49 patients who did not undergo angiography were excluded from further analysis, leaving 116 patients in the study who received all three tests (computerized 2-lead resting ECG, SPECT MPI). The sensitivity and specificity of the computerized 2-lead resting ECG was 91% (95% CI: 0.79-0.97) and 87% (95% CI: 0.76-0.94) respectively, compared to a sensitivity and specificity of 85% (95% CI 0.72-0.93) and 14% (95% CI 0.07-0.25) respectively, 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 including 1,323 individuals, the pooled estimate for specificity of SPECT was 0.77 (95% CI: 0.64-0.86), and the pooled sensitivity was 0.83 (CI: 0.81-0.91).⁷ The reduced specificity reported in the Strobeck study may have been related to the performance of angiography in patients with valvular disease, since these patients may have higher rates of false-positive SPECT exams compared to patients with suspected ischemia.

Two smaller studies of diagnostic accuracy were published in 2014 and 2015.^{8,9} 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 one 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 of 91.2% and specificity of 84.6%. However, most published studies have methodologic limitations that reduce their internal validity. In all but one, the population was a convenience sample of patients who underwent angiography. These patient populations are thus subject to a referral or “workup” bias in that the population

of patients that might be considered for the computerized 2-lead resting ECG 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 1 cohort, 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 demonstrated how computerized 2-lead resting ECG analysis can be used to change clinical management in ways that improve health outcomes. Moreover, given the 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. Relevant outcomes include 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 of participant's exclusion from analyses. These methodologic limitations create a substantial degree of uncertainty concerning 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 nonacute setting, the most common method for diagnosing CAD is stress testing, and there is no evidence comparing the diagnostic accuracy of computerized 2-lead electrocardiogram analysis with stress testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

A search of [ClinicalTrials.gov](https://clinicaltrials.gov) did not identify any ongoing or unpublished trials that would likely influence this review.

SUPPLEMENTAL INFORMATION

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 recommendations for computerized 2-lead resting electrocardiogram analysis have been identified.

Government Regulations

National/ Local:

There is no national coverage determination.

WPS, L35490, Category III CPT® Codes, for services performed on or after 11/01/2019.

Group 1 Paragraph: The Category III CPT codes listed below are considered not medically necessary:

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.

*Code was deleted effective 12/31/2019

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. Strobeck JE, Shen JT, Singh B, et al. Comparison of a two-lead, computerized, resting ECG signal analysis device, the MultiFunction-CardioGram or MCG (a.k.a. 3DMP), to quantitative coronary angiography for the detection of relevant coronary artery stenosis (>70%) - a meta-analysis of all published trials performed and analyzed in the US. Int J Med Sci. 2009;6(4):143-155. PMID 19381351
2. Grube E, Bootsvelde A, Yuecel S, et al. Computerized two-lead resting ECG analysis for the detection of coronary artery stenosis. Int J Med Sci. 2007;4(5):249-263. PMID 18026565
3. Grube E, Bootsvelde 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. PMID 18345283

4. 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.* Jan-Feb 2002;4(1):2-12. PMID 11975826
5. Hosokawa J, Shen JT, Imhoff M. Computerized 2-lead resting ECG analysis for the detection of relevant coronary artery stenosis in comparison with angiographic findings. *Congest Heart Fail.* Sep-Oct 2008;14(5):251-260. PMID 18983288
6. Strobeck JE, Mangieri A, Rainford N. A paired-comparison of the Multifunction Cardiogram (MCG) and sestamibi SPECT myocardial perfusion imaging (MPI) to quantitative coronary angiography for the detection of relevant coronary artery obstruction ($\geq 70\%$) - a single-center study of 116 consecutive patients referred for coronary angiography. *Int J Med Sci.* 2011;8(8):717-724. PMID 22135619
7. de Jong MC, Genders TS, van Geuns RJ, et al. Diagnostic performance of stress myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis. *Eur Radiol.* Sep 2012;22(9):1881-1895. PMID 22527375
8. Amano T, Shinoda N, Kunimura A, et al. Non-invasive assessment of functionally significant coronary stenoses through mathematical analysis of spectral ECG components. *Open Heart.* 2014;1(1):e000144. PMID 25469309
9. Kawaji T, Shiomi H, Morimoto T, et al. Noninvasive detection of functional myocardial ischemia: Multifunction Cardiogram Evaluation in Diagnosis of Functional Coronary Ischemia Study (MED-FIT). *Ann Noninvasive Electrocardiol.* Sep 2015;20(5):446-453. PMID 25594689

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through December 2019, the date the research was completed.

Joint BCBSA/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/10	5/13/10	4/20/10	Joint policy established
5/1/12	2/21/12	2/21/12	Routine maintenance; references added, description updated and policy changed BCBSA policy. Title changed from “Algorithmic Analysis of ECG-Derived Data” to “Computerized 2-lead Resting Electrocardiogram Analysis for the Diagnosis of Coronary Artery Disease”.
9/1/13	6/19/13	6/26/13	Routine maintenance. No change in policy status.
5/1/15	2/17/15	2/27/15	Routine maintenance
5/1/16	2/16/16	2/16/16	Routine maintenance
5/1/17	2/21/17	2/21/17	Routine maintenance, updated rationale section, added references 8, 9.
5/1/18	2/20/18	2/20/18	Routine policy maintenance. No changes in policy status.
5/1/19	2/19/19		Routine policy maintenance. No change in policy status.
5/1/20	2/18/20		Routine policy maintenance. Code 0206T deleted effective 12/31/19, no replacement code. Policy recommended for retirement.

Next Review Date: Computerized 2-lead ECG has been determined to be obsolete and is no longer subject to routine review.

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: COMPUTERIZED 2-LEAD RESTING ELECTROCARDIOGRAM ANALYSIS FOR THE
DIAGNOSIS OF CORONARY ARTERY DISEASE

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered.
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

N/A