

Corporate Medical Policy

Myocardial Sympathetic Innervation Imaging

File Name: myocardial_sympathetic_innervation_imaging
Origination: 7/2013
Last Review: 5/2024

Description of Procedure or Service

In patients with heart failure, activation of the sympathetic nervous system is an early mechanism to compensate for decreased myocardial function. The concentration of 123Iodine meta-iodobenzylguanidine (MIBG) over several hours after injection of the agent is a potential marker of sympathetic neuronal activity and may correlate with the severity of heart failure. MIBG activity is proposed as a prognostic marker in patients with heart failure to aid in the identification of patients at risk of 1- and 2-year mortality. The marker could also potentially be used to guide treatment decisions or to monitor the effectiveness of heart failure treatments.

Background

An estimated 6.2 million adults in the U.S. have heart failure. In 2018, heart failure was mentioned on 379,800 death certificates in the U.S. Underlying causes of heart failure include coronary artery disease (CAD), hypertension, valvular disorders, and primary cardiomyopathies. These conditions reduce myocardial pump function and decrease left ventricular ejection fraction (LVEF). An early mechanism to compensate for this decreased myocardial function is activation of the sympathetic nervous system. The increased sympathetic activity initially helps compensate for heart failure by increasing heart rate and myocardial contractility in order to maintain blood pressure and organ perfusion. However, over time, this places additional strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease and/or myocardial damage. As the ability of the heart to compensate for reduced myocardial function diminishes, clinical symptoms of heart failure develop. Another detrimental effect of heightened sympathetic activity is an increased susceptibility to potentially fatal ventricular arrhythmias.

Overactive sympathetic innervation associated with heart failure involves increased neuronal release of norepinephrine (NE), which is the main neurotransmitter of the cardiac sympathetic nervous system. In response to sympathetic stimulation, vesicles containing NE are released into the neuronal synaptic cleft. The released NE binds to post-synaptic beta-1, beta-2 and alpha receptors, enhances adenylyl cyclase activity and brings about the desired cardiac stimulatory effects. NE is then taken back into the presynaptic space for storage or catabolic disposal that terminates the synaptic response by the uptake-1 pathway. The increased release of NE is usually accompanied by decreased NE reuptake, thereby further increase circulating NE levels.

Guanethidine is a false neurotransmitter that is an analogue of NE; it is also taken up by the uptake-1 pathway. 123Iodine meta-iodobenzylguanidine (¹²³I-MIBG or MIBG) is guanethidine that is chemically modified and labeled with radioactive iodine. MIBG moves into the synaptic cleft and then is taken up and stored in the presynaptic nerve space in a manner that is similar to NE. However, unlike NE, MIBG is not catabolized and thus concentrates in myocardial sympathetic nerve endings. This concentrated MIBG can be imaged with a conventional gamma camera. The concentration of MIBG over several hours after injection of the agent is thus a reflection of sympathetic neuronal activity, which in turn may correlate with the severity of heart failure.

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MIBG myocardial imaging has been in use in Europe and Japan and standardized procedures for imaging have been proposed by European organizations. Administration of MIBG is recommended by slow (1 to 2 minutes) injection. Planar images of the thorax are acquired 15 minutes (early image) and 4 hours (late image) after injection. In addition, optional single-photon emission computed tomography (SPECT) imaging can be performed following the early and late planar images. MIBG uptake is semi-quantified by determining the average count per pixel in regions of interest (ROI) drawn over the heart and the upper mediastinum in the planar anterior view. There is no single universally used myocardial MIBG index. The most commonly used myocardial MIBG indices are the early heart to mediastinum (H/M) ratio, late H/M ratio and the myocardial MIBG washout rate. The H/M ratio is calculated by taking the average count per pixel in the myocardium divided by the average count per pixel in the mediastinum. The myocardial washout rate is expressed as the rate of decrease in myocardial counts over time between early and late imaging (normalized to mediastinal activity).

MIBG activity is proposed as a prognostic marker in patients with heart failure, to be used in conjunction with established markers or prognostic models to identify heart failure patients at increased risk of short-term mortality. MIBG activity could also potentially be used to guide treatment decisions or to monitor the effectiveness of heart failure treatments.

Regulatory Status

In 2008, AdreView[®] (Iobenguane I 123) Injection (GE Healthcare) was approved by the Food and Drug Administration new drug application process (22-290) for the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.

In 2013, the Food and Drug Administration approved a supplemental new drug application (22-290/S-001) for AdreView[®] and expanded the labeled indication to include scintigraphic assessment of sympathetic innervation of the myocardium by measurement of the H/M ratio of radioactivity uptake in patients with New York Heart Association class II or class III heart failure and left ventricular ejection fraction less than 35%.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Myocardial sympathetic innervation imaging with ¹²³Iodine meta-iodobenzylguanidine (MIBG) is considered investigational for patients with heart failure.

BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Myocardial sympathetic innervation imaging is covered

Not applicable.

When Myocardial sympathetic innervation imaging is not covered

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Policy Guidelines

For individuals with heart failure who receive imaging with iodine 123 meta-iodobenzylguanidine (MIBG) for prognosis, the evidence includes numerous studies that MIBG cardiac imaging findings predict outcomes in patients with heart failure. Relevant outcomes are overall survival, disease-specific survival, functional outcomes, health status measures, quality of life, hospitalizations, and medication use. While the available studies vary in their patient inclusion criteria and methods for analyzing MIBG parameters, the highest quality studies demonstrate a significant association between MIBG imaging results and adverse cardiac events, including cardiac death. Moreover, MIBG findings have been shown to improve the ability of the Seattle Heart Failure Model and other risk models to predict mortality. However, there is no direct published evidence on the clinical utility of MIBG (i.e., whether findings of the test would lead to patient management changes that improve health outcomes) and no clear chain of indirect evidence of clinical utility. Management changes made as a result of MIBG imaging are uncertain, and it is not possible to determine whether management changes based on MIBG results lead to superior outcomes compared with management without MIBG imaging. The evidence is insufficient to determine the effects of the technology on health outcomes.

American Heart Association et al

The American Heart Association, American College of Cardiology, and Heart Failure Society of America published joint guidelines on the management of heart failure in 2022. These guidelines did not address the use of MIBG imaging in heart failure management.

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (2011) published a report on the translation of cardiovascular molecular imaging. In regard to heart imaging with meta-iodobenzylguanidine (MIBG), the report cited the ADMIRE-HF trial, and stated that additional clinical trials would be needed to determine the efficacy of heart failure management strategies using MIBG compared with usual care without MIBG imaging.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 0331T, 0332T, A9582

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 6/13/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 6/12/14

Specialty Matched Consultant Advisory Group, 7/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 6/11/15

Specialty Matched Consultant Advisory Panel 6/2015

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BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 9/8/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 9/13/2018

Specialty Matched Consultant Advisory Panel 5/2020

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 9/12/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.56, 9/10/2020

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Medical Director review 5/2021

Buxton DB, Antman M, Danthi N, et al. Report of the National Heart, Lung, and Blood Institute working group on the translation of cardiovascular molecular imaging. *Circulation*. May 17 2011; 123(19): 2157-63. PMID 21576680

Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation*. Aug 08 2017; 136(6): e137-e161. PMID 28455343

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Food and Drug Administration (FDA). Approval letter: NDA 22-290. *AdreView*, (Iobenguane I 123) 2mCi/mL Injection. 2008; https://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/022290s000toc.cfm.

Food and Drug Administration (FDA). Supplemental Approval letter: NDA 22-290/S-001. *AdreView* (Iobenguane I 123) Injection. 2013; https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/022290orig1s001ltr.pdf.

Centers for Disease Control and Prevention (CDC). Heart Failure. 2020; https://www.cdc.gov/heartdisease/heart_failure.htm.

Chirumamilla A, Travin MI. Cardiac applications of 123I-mIBG imaging. *Semin Nucl Med*. Sep 2011; 41(5): 374-87. PMID 21803188

Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. May 03 2022; 79(17): e263-e421. PMID 35379503

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Centers for Disease Control and Prevention (CDC). Heart Failure. 2023; https://www.cdc.gov/heartdisease/heart_failure.htm.

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Jacobson AF, Senior R, Cerqueira MD, et al. Myocardial iodine-123 meta-iodobenzylguanidine imaging and cardiac events in heart failure. Results of the prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) study. J Am Coll Cardiol. May 18 2010; 55(20): 2212-21. PMID 20188504

Specialty Matched Consultant Advisory Panel 5/2024
Medical Director review 5/2024

Policy Implementation/Update Information

- 7/30/13 New policy developed. Myocardial sympathetic innervation imaging with ¹²³Iodine meta-iodobenzylguanidine (MIBG) is considered investigational for patients with heart failure. Medical Director review 7/2013. (sk)
- 8/13/13 Removed codes 0031T and 0032T from Billing/Coding section. Added codes 0331T and 0332T to Billing/Coding section. (sk)
- 8/12/14 Reference added. Specialty Matched Consultant Advisory Panel review 7/29/14. No change to Policy statement. (sk)
- 7/28/15 Updated Policy Guidelines section. Reference added. Specialty Matched Consultant Advisory Panel review 6/24/2015. No change to policy statement. (lpr)
- 7/26/16 Specialty Matched Consultant Advisory Panel review 6/29/2016. No change to policy statement. (an)
- 6/30/17 Updated Policy Guidelines section. Reference added. Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (an)
- 6/29/18 Specialty Matched Consultant Advisory Panel review 5/23/2018. No change to policy statement. (an)
- 6/11/19 Description section updated. Reference added. Specialty Matched Consultant Advisory Panel review 5/15/2019. No change to policy statement. (an)
- 6/9/20 Reference added. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 5/20/2020. No change to policy statement. (eel)
- 06/1/21 Reference added. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 5/2021. Medical Director review. No change to policy statement. (bb)
- 5/31/22 References added. Related policies updated. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 5/2022. Medical Director review 5/2022. No change to policy statement. (tt)
- 5/30/23 References added. Policy Guidelines and description updated. Specialty Matched Consultant Advisory Panel review 5/2023. Medical Director review 5/2023. No change to policy statement. (tt)
- 5/29/24 References added. Specialty Matched Consultant Advisory Panel review 5/2024. Medical Director review 5/2024. No change to policy statement. (tt)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.