MEDICAL POLICY – 6.01.56
Myocardial Sympathetic Innervation Imaging in Patients with Heart Failure

Introduction

An MIBG scan involves injecting a radioactive material (iodine-123-meta-iodobenzylguanidine) into the body. This radioactive material — known as a tracer — gathers in specific nerve endings in the heart. The tracer gives off gamma rays, which can be detected by a special type of scanner. The goal is to try to determine the severity of heart failure and who could be at high risk of dying from it in 1 to 2 years. It’s also been proposed that MIBG scans could someday help guide treatment for and monitoring of heart failure. Medical studies have not been able to determine if MIBG test results lead to better health outcomes. For this reason MIBG scans are considered investigational (unproven) for patients with heart failure.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
Myocardial sympathetic innervation imaging with Iodine123 meta-iodobenzylguanidine (MIBG) is considered investigational for patients with heart failure.

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT</td>
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<tr>
<td>0331T</td>
<td>Myocardial sympathetic innervations imaging; planar qualitative and quantitative assessment</td>
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<tr>
<td>0332T</td>
<td>Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment; with tomographic SPECT</td>
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<td>HCPCS</td>
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<td>A9582</td>
<td>Iodine I-123 iobenguane, diagnostic, per study dose, up to 15 millicuries</td>
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### Related Information

N/A

### Evidence Review

### Description

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

Background

Heart Failure

An estimated 5.7 million adults in the United States have heart failure, which is the main cause of death for approximately 58,300 Americans each year. Underlying causes of heart failure include coronary artery disease, hypertension, valvular disorders, and primary cardiomyopathies. These conditions reduce myocardial pump function and decrease left ventricular ejection fraction. 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 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), 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 postsynaptic β₁, β₂, and α receptors, enhances adeny 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 increasing circulating NE levels.

Diagnostic Imaging

Guanethidine is a false neurotransmitter that is an analog of NE; it is also taken up by the uptake-1 pathway. Iodine 123 meta-iodobenzylguanidine (¹²³I-MIBG or MIBG) is chemically modified guanethidine 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 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.

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 (1-2 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 can be performed following the early and late planar images. MIBG uptake is semiquantified by determining the average count per pixel in regions of interest 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 be used to guide treatment decisions or to monitor the effectiveness of heart failure treatments.

**Summary of Evidence**

For individuals with heart failure who receive imaging with MIBG for prognosis, the evidence includes numerous studies that MIBG cardiac imaging findings predict outcomes in patients with heart failure. The 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 have demonstrated 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 (ie, whether findings of the test would lead to patient management changes that improve health outcomes) and no chain of evidence can be constructed to support 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 improved health outcomes compared with management without MIBG imaging. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in July 2019 showed no relevant clinical trials.

Practice Guidelines and Position Statements

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (2011) published a report on the translation of cardiovascular molecular imaging.23 In regard to heart imaging with meta-iodobenzylguanidine (MIBG), the report cited the ADMIRE-HF trial9 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.

American College of Cardiology Foundation et al

The American College of Cardiology Foundation and the American Heart Association updated its 2013 joint guidelines (2017) on the management of heart failure with the Heart Failure Association of America.24 These guidelines did not address the use of MIBG imaging in heart failure management.

Medicare National Coverage

There is no national coverage determination.
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.4

The Food and Drug Administration (2013) approved a supplemental new drug application (22-290/S-01) 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%.5

References


History

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<td>08/12/13</td>
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<td>08/11/14</td>
<td>Annual Review. Policy updated with literature review through May 13, 2014; references 8, 12, 15, 16 added; others renumbered/removed. Policy statements unchanged. Related Policies updated; 2.04.32 removed; it has been archived.</td>
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<td>01/19/16</td>
<td>Coding Update. New CPT code 0399T, effective 1/1/16, added to policy.</td>
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<td>03/31/16</td>
<td>Coding Update. CPT code 0399T removed, CPT code previously added in error.</td>
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<td>Update Related Policies. Removed 12.04.67 as it was deleted; information moved to 2.04.509.</td>
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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
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