Autonomic nervous system monitoring for neuropathy

Clinical Policy ID: CCP.1005

Recent review date: 4/2021

Next review date: 8/2022

Policy contains: Autonomic nervous system; diabetes; diagnosis; neuropathy.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Sandhills Center when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Sandhills Center clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

Autonomic nervous system testing and monitoring is clinically proven and, therefore, medically necessary for neuropathy when overseen and interpreted by a physician of the appropriate specialty (neurologist or cardiologist); to evaluate symptoms of vasomotor instability (e.g., hypotension, orthostatic tachycardia, and hyperhidrosis) after more common causes have been excluded; and to achieve a more definitive diagnosis to improve medical decision making for any of the following goals (Centers for Medicare & Medicaid Services Local Coverage Determinations L33609, L35124, and L35395; Cheshire, 2020):

- To diagnose the presence of autonomic neuropathy when signs or symptoms suggest a progressive autonomic neuropathy.
- To evaluate the severity and distribution of a diagnosed progressive autonomic neuropathy.
- To differentiate certain complicated variants of syncope from other causes of loss of consciousness.
- To evaluate inadequate response to beta blockade in vasodepressor syncope.
- To diagnose symptoms suspicious for distal small fiber neuropathy.
- To differentiate the cause of postural orthostatic tachycardia syndrome.
- To evaluate a change in type, distribution, or severity of autonomic deficits in members with autonomic failure.

- To evaluate treatment response in members with autonomic failure who demonstrate a change in clinical exam.
- To diagnose symptomatic axonal neuropathy or suspected autonomic neuropathy.
- To evaluate and treat members with recurrent unexplained syncope to demonstrate autonomic failure, after more common causes have been excluded by other standard testing.

Limitations

All other uses of autonomic nervous system monitoring for neuropathy are not medically necessary.

Alternative covered services

- Physician office visits.
- Appropriate therapy sessions.

Background

The autonomic nervous system, which consists of the sympathetic and parasympathetic systems, regulates physiologic processes without conscious control (Mayo Clinic, 2020). The autonomic nervous system affects blood pressure, heart rate, body temperature, digestion, metabolism, fluid and electrolyte balance, sweating, urination, defecation, sexual response, and other processes.

Disorders of the autonomic nervous system, including neuropathy, can be primary or secondary to other disorders (Cleveland Clinic, 2016). Symptoms indicative of autonomic nervous system disorders are multiple; such symptoms can include orthostatic hypotension, heat intolerance, nausea, constipation, urinary retention or incontinence, nocturia, impotence, and dry mucous membranes.

An autonomic nervous system dysfunction that affects the cardiovascular system may result in either rapid resting or slowing heart rate. Blood pressure may drop on standing, a condition called “orthostatic hypotension.” Any cardiovascular effects may result in syncope, or loss of consciousness. An autonomic nervous system dysfunction affecting other organs may result in genitourinary symptoms (e.g., urinary incontinence, erectile dysfunction, or incomplete voiding/neurogenic bladder); gastrointestinal symptoms (gastroparesis, diarrhea, or constipation); sweating problems with excessive or inadequate sweat production that can affect body temperature control; or vision difficulties from inappropriate pupillary constriction.

Many factors can cause autonomic nervous system neuropathy. Primary causes include familial dysautonomia (Riley-Day syndrome), idiopathic orthostatic hypotension (progressive autonomic failure), multiple system atrophy with autonomic failure (Shy-Drager syndrome), and Parkinson’s syndrome with autonomic failure. More than one million Americans are impacted by a primary cause (Mayo Clinic, 2020). There are numerous secondary causes, including specific disorders such as diabetes mellitus, Lyme disease, and human immunodeficiency virus, or general dysfunctions such as physical trauma, surgery, pregnancy, or viral illness (Cleveland Clinic, 2016).

Autonomic neuropathy is an important, but not well-recognized complication of diabetes. Its clinical manifestations include orthostatic hypotension, exercise intolerance, gastroparesis, diarrhea, constipation, and urinary incontinence. The disorder is linked with sudden unexplained deaths in young people, even though the condition is relatively rare. In diabetic adults, autonomic neuropathy is a strong predictor of mortality, mostly due to cardiovascular disease, nephropathy, and hypoglycemia (Tang, 2013).

Autonomic nervous system testing includes three domains (Centers for Medicare & Medicaid Services Local Coverage Determination L35395, 2019):

- Cardiovagal innervation is a test that provides a standardized quantitative evaluation of vagal innervation to parasympathetic function of the heart. Responses are based on the interpretation of changes in continuous heart recordings in response to standardized maneuvers and include heart rate response to deep breathing, Valsalva ratio, and 30:15 ratio heart rate responses to standing. A tilt table may be used, but is not required.
- Vasomotor adrenergic innervation evaluates adrenergic innervation of the circulation and of the heart in autonomic failure. The following tests are included: beat-to-beat blood pressure and R-R interval response to Valsalva maneuver, sustained hand grip, and blood pressure and heart rate responses to tilt-up or active standing and must be performed with a tilt table.
- Sudomotor function testing evaluates and documents neuropathic disturbances that may be associated with pain. The quantitative sudomotor axon reflex test, thermoregulatory sweat test, sympathetic skin responses, and silastic sweat imprints are tests of sympathetic cholinergic sudomotor function.

Findings

The Centers for Medicare & Medicaid Services issued a Local Coverage Determination, effective November 2017, listing criteria (goals) for testing the autonomic nervous system and subsequent monitoring (U.S. Centers for Medicare & Medicaid Services, 2019). These criteria are specified in the coverage section of this policy.

An American Academy of Neurology (2009) practice parameter found that autonomic testing should be considered in evaluating patients with polyneuropathy to document autonomic nervous system involvement and suspected autonomic neuropathies. Both applications were given a level “B” grade by the expert panel, which was defined as “probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population.”

Recommendations from the Neuropathy Study Group of the Italian Society of Diabetology were produced because diabetic autonomic neuropathy is not often diagnosed. These recommendations include information on how and when to perform the recommended cardiovascular tests, and how to interpret them (Spallone, 2011).

Diabetic autonomic neuropathy is common among diabetics, and raises the morbidity and mortality risk in older adults as it often goes undiagnosed and untreated (Scheinberg, 2016). One study of 151 participants with type 1 diabetes assessed the association of various risk factors to the disease, including neuropathy and diabetic neuropathy, and both were highly significant predictors of the disease (Tannus, 2014). Another review (Rolim, 2013) found an under-diagnosis of cardiovascular autonomic neuropathy in participants with diabetes due to low interest in an unfamiliar complication, skepticism of therapies, lack of understanding diagnostic utility, and need for education and training — in spite of evidence of predictive value of neuropathy for the disease. A related issue was the lack of uniformity of treatment.

A study of 490 persons ages 50 – 75 with diabetes followed for a median of 13.6 years found that cardiac autonomic dysfunction, described using 10 measures, was strongly associated with a risk of cardiovascular mortality. The study recommended such measures be monitored in persons with diabetes (Beijers, 2009). A related article found that the impact of hypoglycemia on cardiovascular autonomic function could explain the risk of cardiovascular mortality among persons with diabetes (Adler, 2009). Another study documented that more persons with diabetes on intensive therapy had neuropathy than those on standard therapy (Duckworth, 2009).

A systematic review of eight studies determined that heart rate variability is a reasonably effective tool in the diagnosis and prognosis of diabetes mellitus (sensitivity 72% to 100%, specificity 71% to 97%), and can be used as an adjunct to standard autonomic tests (Franca da Silva, 2016).

Risk factors for cardiac autonomic neuropathy were analyzed in a meta-analysis of four studies (n = 1,755). Factors that significantly raised risk included age, duration of diabetes, body mass index, proliferative retinopathy, microalbuminuria, hypertension, systolic and diastolic blood pressure, HbA1C, triglycerides, and high-density lipoprotein cholesterol. Findings allow practitioners to identify persons with diabetes at high risk of developing cardiac autonomic neuropathy (Dafaalla, 2016).

A systematic review (Bento, 2017) of 18 retrospective and prospective cohort studies (n = 6,915) addressed monitoring of invasive and non-invasive heart rate variability as a potentially useful tool in addition to conventional autonomic tests in intensive care units. Results included increases in mortality associated with reduction in variability (entropy 0.65 versus 0.84, $P < .05$); reduction in the baroreflex (transfer) function (0.43 versus 1.11, $P < .05$); sustained reduction of the low frequency/high frequency ratio (0.22 versus 0.62, $P < .01$); loss of heart rate volatility during the first 24 hours of hospitalization; and reduction in variability in patients admitted to intensive care after cardiac arrest and undergoing therapeutic hypothermia.

A systematic review of 11 studies showed that documenting abnormal heart rate variability in patients with systemic lupus erythematosus reflects cardiac autonomic dysfunction (Matusik, 2018). Thus, heart rate can be a useful tool for monitoring autonomic dysfunction in the disease, and generate useful prognostic information.

Individuals with metabolic syndrome have alterations in the function of the autonomic nervous system, and these alterations are linked with greater risk of aspects of the syndrome, such as obesity, hypertension, and insulin resistance — although the issue of whether these alterations are contributors or a consequence of the syndrome remains unresolved (Licht, 2010).

A review of 127 patients in 90 newly diagnosed type 2 diabetic patients and 37 patients with normal glucose tolerance were given Ewing tests and continuous glucose monitoring (Xu, 2017). The prevalence of cardiovascular autonomic neuropathy in newly-diagnosed diabetes was low (22.2%), while those with the greatest glycemic variability had the highest prevalence of cardiovascular autonomic neuropathy; thus glycemic variability can be a helpful method of identifying neuropathy.

In 2019, we updated the policy references and changed the policy ID from CP# 09.01.01 to CCP.1005.

In 2020, we added one professional guidance statement on testing for autonomic and somatic nerve dysfunction (Vinik, 2017) and two Local Coverage Determinations (L35124 and L33609) to the policy and deleted three references from the policy (Brown, 2009; Del Buono, 2016; Lauer, 2009), resulting in no changes to the policy.

In 2021, we added a new guideline on electrodiagnostic assessment of the autonomic nervous system (Cheshire, 2020). The recommendations for testing are consistent with this policy, and no coverage changes are warranted.

References

On January 14, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Autonomic Nervous System Diseases/diagnosis” (MeSH), “autonomic nervous system,” and “neuropathy.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

2/2013: initial review date and clinical policy effective date: 9/2013

8/2016: Policy references updated.

4/2017: Policy references updated.

4/2018: Policy references updated.

4/2019: Policy references updated.

4/2020: Policy references updated.

4/2021: Policy references updated.