Policy Replaced with LCD L34555
Effective February 26, 2018

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Ultrasonographic Measurement of Carotid Intimal-Medial Thickness as an Assessment of Subclinical Atherosclerosis

Policy #: 245
Category: Medicine

Latest Review Date: January 2017
Policy Grade: C

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:

Ultrasonographic measurement of carotid intima-medial (or intimal-media) thickness (CIMT) refers to the use of B-mode ultrasound to determine the thickness of the two innermost layers of the carotid artery wall, the intima and the media. Detection and monitoring of intima-medial thickening, which is a surrogate marker for atherosclerosis, may provide an opportunity to intervene earlier in atherogenic disease and/or monitor disease progression.

Coronary heart disease (CHD) accounts for 30.8% of all deaths in the United States. Established major risk factors for CHD have been identified by the National Cholesterol Education Program (NCEP) Expert Panel. These risk factors include elevated serum levels of low density lipoprotein (LDL) cholesterol, total cholesterol, and reduced levels of high-density lipoprotein (HDL) cholesterol. Other risk factors include a history of cigarette smoking, hypertension, family history of premature CHD, and age.

The third report of the NCEP Adult Treatment Panel (ATP III) establishes various treatment strategies to modify the risk of CHD, with emphasis on target goals of LDL cholesterol. Pathology studies have demonstrated that levels of traditional risk factors are associated with the extent and severity of atherosclerosis. ATP III recommends the use of the Framingham criteria to further stratify those patients with two or more risk factors for more intensive lipid management.

However, at every level of risk factor exposure, there is substantial variation in the amount of atherosclerosis, presumably related to genetic susceptibility and the influence of other risk factors. Therefore, there has been interest in identifying a technique that can improve the ability to diagnose those at risk of developing CHD, as well as measure disease progression, particularly for those at intermediate risk.

The carotid arteries can be well visualized by ultrasonography, and ultrasonographic measurements of the thickness of the carotid intimal-medial wall (CIMT) have been investigated as a technique to identify and monitor subclinical atherosclerosis. B-mode ultrasound is most commonly used, and the intimal-medial thickness is measured and averaged over several sites in each carotid artery. Imaging of the far wall of each common carotid artery yields more accurate and reproducible IMT measurements than imaging of the near wall. Two echogenic lines are produced, representing the lumen-intima interface and the media-adventitia interface. The distance between these two lines constitutes the IMT.

Policy:

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

Effective for dates of service on or after March 12, 2006 and prior to February 26, 2018:
Blue Advantage will treat **ultrasonographic measurement of carotid artery intimal-medial thickness (CIMT)** as a technique for identifying subclinical atherosclerosis for use in the screening, diagnosis, or management of atherosclerosis 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 performed through December 15, 2016.

Measurement of carotid intima-medial (or intimal-media) thickness (CIMT) is primarily meant to assess risk for future disease, and therefore can be evaluated as a prognostic measure. Assessment of a prognostic measure typically focuses on three categories of evidence: (1) its technical performance; (2) prognostic value (i.e., statistically significant association between the test result and health outcomes); and (3) impact on health outcomes (i.e., demonstration that use of the prognostic information clinically can alter clinical management and/or improve health outcomes compared with patient management without use of the prognostic tool). In some cases, it is important to evaluate whether the test provides incremental information above the standard workup in order to determine whether the test has utility in clinical practice.

The literature on the use of carotid intima-media thickness for cardiac risk stratification consists of numerous cohort studies and systematic reviews of these cohort studies. The following review includes the largest prospective cohort studies and the most important systematic reviews of these studies.

Prognostic Utility

Systematic reviews

A 2013 meta-analysis of 15 articles by van den Oord et al found similar results on the added value of CIMT. Six cohort studies totaling 32,299 patients were evaluated to examine the value of CIMT added to traditional cardiovascular risk factors. While a CIMT increase of 0.1mm was predictive for MI (HR=1.15; 95% CI, 1.12 to 1.18) and for stroke (HR=1.17; 95% CI, 1.15 to 1.21), the addition of CIMT did not statistically significantly increase risk prediction over traditional cardiovascular risk factors (p=0.8).

In a 2012 meta-analysis, the USE Intima-Media Thickness (USE-IMT) collaboration, investigators sought to determine whether common carotid intima-media thickness (CIMT) measurements could assist in estimating the ten year risk of first-time myocardial infarction (MI) or first-time stroke when added to the Framingham Risk Score. Using individual data for 45,828 patients from 14 population-based cohort studies, Den Ruijter et al found risk of first-time MI or stroke was related positively to both the Framingham Risk Score and the adjusted common CIMT. The mean common CIMT was 0.73 mm and increased in every cohort with patient age during a median follow-up of 11 years. For every 0.1 mm difference in common CIMT, the hazard ratio (HR) for risk of MI or stroke, which occurred in 4007 patients, was 1.12 (95% confidence interval [CI], 1.09 to 1.14) for women and 1.08 (95% CI, 1.05 to 1.11) for men. However, adding common CIMT measurements to the Framingham Risk Score did not improve risk prediction and resulted in reclassification of risk in only 6.6% of patients. The added value of mean common CIMT in reclassifying risk was only 0.8% (95% CI, 0.1% to 1.6%) and did not differ between men and women. The c-statistic of the Framingham Risk Score model with and without CIMT was similar (0.759; 95% CI, 0.752 to 0.766; and 0.757; 95% CI, 0.749 to 0.764), suggesting the addition of CIMT in risk assessment offered limited benefit.

In a 2012 meta-analysis of individual participant data pooled from 16 studies with a total of 36,984 patients, Lorenz et al examined CIMT progression from two ultrasound screenings taken two to seven years apart (median, four years). Patients were followed for a mean of seven years, during which time 1339 strokes, 1519 MI, and 2028 combined end points (MI, stroke, vascular death) occurred. The mean CIMT of the two ultrasound results was predictive of cardiovascular risk using the combined end point (adjusted HR=1.16; 95% CI 1.10 to 1.22). In sensitivity analyses, no associations were found between cardiovascular risk and individual CIMT progression regardless of CIMT definition, end point, and adjustments. As an example, for the combined end points, an increase of 1 SD in mean common CIMT progression resulted in an overall estimated HR of 0.97 (95% CI, 0.94 to 1.00) when adjusted for age, sex, and mean common CIMT, and HR was 0.98 (95% CI, 0.95 to 1.01) when adjusted for vascular risk factors. These data confirm that CIMT is a predictor of cardiovascular risk, but do not demonstrate that changes in CIMT over time are predictive of future events.

In 2010, Mookadam et al conducted a systematic review of the role of CIMT in predicting individual cardiovascular event risk and as a tool in assessing therapeutic interventions. The authors concluded that CIMT is an independent risk factor for cardiovascular events and may be useful in determining treatment when there is uncertainty regarding the approach or patient reluctance. However, further studies are needed to identify the best approaches to screening and interventions to prevent progression of atherosclerosis.

Studies have found including carotid plaques in CIMT increases the predictive value of cardiovascular risk over CIMT assessed only in plaque-free sites. However, the meta-analysis by Lorenz found no difference in the main results between studies that included CIMT with carotid plaque and plaque-free CIMT. The 2012 systematic review by Peters found adding carotid plaque to the traditional CIMT model increased the c-statistic from 0.01 to 0.06.

Prospective cohort studies

Numerous prospective cohort studies have evaluated the association of CIMT with future cardiovascular events. Some of the larger trials are discussed below.

In the Atherosclerosis Risk in Communities (ARIC) study, the authors evaluated risk factors associated with increased CIMT in 15,800 subjects. CIMT had a graded relationship with increasing quartiles of plasma total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. CIMT was then also correlated with the incidence of CHD in a subgroup of patients enrolled in the trial after four to seven years of follow-up. Among the 12,841 subjects studied, there were 290 incident events. The HR rate for men and women, adjusted for age and gender, comparing extreme CIMT (i.e., ≥1 mm) to non-extreme CIMT (i.e., <1 mm) was 5.07 for women and 1.85 for men. The strength of the relationship was reduced by including major coronary heart disease (CHD) risk factors but remained elevated for higher measurements of CIMT. The authors concluded that mean CIMT is a noninvasive predictor of future CHD incidence.

The Rotterdam study was a prospective cohort study that started in 1989 and recruited 7983 men and women aged 55 years and older. The main objective of the Rotterdam study was to investigate the prevalence and incidence of risk factors for chronic diseases, including cardiovascular disease, in elderly people. One aspect of the study sought to determine whether progression of atherosclerosis in asymptomatic elderly subjects is a prelude to cardiovascular events. Measurements of CIMT were used to assess the progression of atherosclerosis. Increasing CIMT was associated with increasing risks of stroke and MI.

O'Leary et al (1999) performed CIMT in 4476 asymptomatic subjects aged 65 years or older without clinical cardiovascular disease in the Cardiovascular Health Study. The incidence of cardiovascular events correlated with measurements of CIMT; this association remained significant after adjustment for traditional risk factors. The authors concluded that increases in CIMT are directly associated with an increased risk of MI and stroke in older adults without a history of cardiovascular disease.

The Carotid Atherosclerosis Progression Study (CAPS) was a longitudinal study of 4904 subjects. All subjects received a baseline CIMT measurement, as well as traditional risk factor analysis, and were followed over a ten year period (mean follow-up, 8.5 years; range 7.1-10.0 years). Adverse outcome events were MI in 73 patients (1.5%), angina or MI in 271 patients (5.5%), and death in 72 subjects (1.5%). Lorenz et al have recently published a retrospective review of the data from CAPS. The authors modeled the predictive value of CIMT on the cardiovascular adverse events within that decade. Because the thresholds of CIMT measurements that would lead to reclassification of risk are unknown, the authors used 24 different models of reclassification and five statistical tests. Each model compares the predictive value of traditional risk factors alone with those risk factors with the addition of CIMT. The authors were unable to find significance in the reclassification models with the addition of CIMT measurements. They concluded that this retrospective analysis does not support the use of CIMT as a clinically useful risk classification tool when used in conjunction with traditional risk factor analysis.

In the Multi-Ethnic Study of Atherosclerosis (MESA) trial, an ongoing cohort study of atherosclerosis, CIMT was found to be a modestly better predictor of stroke but a worse predictor of CHD than coronary artery calcium score at a median follow-up of 3.9 years among 6698 adults asymptomatic at baseline. In a 2010 article from MESA, CIMT results in 4792 healthy, nondiabetic adults who were not on lipid-lowering medications were compared in six different lipid groups, including normolipemic and several types of common dyslipidemias. The mean CIMT values were increased only for the combined hyperlipidemia (defined as any high-density lipoprotein [HDL]-C level, LDL-cholesterol [C] ≥160 and triglyceride ≥150) and simple hypercholesterolemia (defined as any HDL-C level, LDL-C ≥160 and triglyceride <150) groups. In another MESA report, in 2011, on 6760 patients with elevated high-sensitivity C-reactive protein (hsCRP) as defined by the JUPITER study, CIMT increases correlated with obesity but only mildly with hsCRP. A 2015 report from MESA of 6125 individuals with a family history of premature coronary heart disease identified 382 atherosclerotic cardiovascular disease events at a mean follow-up of 10.2 years. The study found that coronary artery calcium improved the risk estimation atherosclerotic cardiovascular disease events but CIMT did not.

In the Bogalusa Heart Study of 991 subjects, obesity along with overweight and elevated metabolic risk were also associated with increased CIMT. In this study population, 41% of patients were found to have increased CHD risk. In the CARDIA study, clotting factor VII was associated with increases in CIMT in 1254 subjects. CIMT is also used as a surrogate outcome measure in atherosclerosis treatment research studies.

In 2010, Raiko et al compared cardiovascular disease risk-scoring tools for identification of CHD risk to CIMT results in 2204 healthy adults, aged 24 to 39 years, from the Cardiovascular Risk in Young Finns study. The cardiovascular disease risk scoring tools evaluated included the Framingham, Reynolds Risk Score, Systematic Coronary Risk Evaluation (SCORE), PROCAM, and Finrisk cardiovascular risk scores. In this population-based follow-up study, the authors found all of the cardiovascular disease risk scores performed equally in being able to predict subclinical atherosclerosis, as measured by high CIMT six years later.

The BioImage study enrolled 5808 asymptomatic individuals from the United States. All patients were evaluated by 3-dimensional carotid ultrasound and by coronary artery calcification score, and followed for a mean of 2.7 years. The primary endpoint was major cardiovascular events, defined as cardiovascular death, MI, and ischemic stroke. The carotid plaque burden was an independent predictor of outcomes, with a hazard ratio of 2.36 (95% CI, 1.13 to 4.92) for individuals in the highest tertile. The coronary calcium score was also an independent predictor of outcomes, with similar hazard ratios to carotid plaque. Both carotid plaque and coronary calcium score led to significant net reclassification, with a net reclassification index of 0.23.

Section Summary: Prognostic Value

Evidence from large, prospective cohort studies has established that CIMT is an independent risk factor for cardiovascular disease. However, systematic reviews have concluded that the ability of CIMT to reclassify patients into clinically relevant categories is modest and may not be clinically important. The uncertainty around the ability to reclassify patients into clinically relevant categories limits the potential for CIMT to improve health outcomes.

Clinical Utility

In a 2011 study by Johnson et al, 355 patients, aged 40 years with one or more cardiovascular disease risk factors, received carotid ultrasound screenings to prospectively determine whether abnormal results would change physician and patient behaviors. Results were considered abnormal (when CIMT was greater than the 75th percentile or the presence of carotid plaque) in 266 patients. Self-reported questionnaires were completed before the carotid ultrasound, immediately after the ultrasound, and 30 days later to determine behavioral changes. Physician behavior in prescribing aspirin and cholesterol medication changed significantly ($p<0.001$ and $p<0.001$, respectively) after identification of abnormal carotid ultrasound results. Abnormal ultrasound results predicted reduced dietary sodium (odds ratio [OR], 1.45; $p=0.002$) and increased fiber intake (OR=1.55; $p=0.022$) in patients but no other significant changes. Health outcomes were not evaluated in this study, and the short-term follow-up limits interpretation of results.

The evidence on reclassification of cardiovascular risk offers a potential indirect chain of evidence to improve outcomes. If a measure is able to reclassify patients into risk categories that have different treatment approaches, then clinical management changes may occur that lead to improved outcomes. Because the ability to reclassify patients into clinically relevant categories with CIMT is modest at best, the clinical utility of this measure for reclassification is uncertain.

Section Summary: Clinical Utility

There is no direct evidence on the clinical utility of measuring CIMT for cardiac risk stratification. The available evidence on reclassification into clinically relevant categories does not support that the use of CIMT will improve health outcomes.

Summary

For individuals who are undergoing cardiac risk assessment who receive ultrasonic measurement of carotid intima-media thickness, the evidence includes large cohort studies and systematic reviews. Relevant outcomes are test accuracy and morbid events. Some studies correlate increased carotid intima-medial thickness (CIMT) with many other commonly used markers for risk of coronary heart disease (CHD) and with risk for future cardiovascular events. A 2012 meta-analysis of individual participant data by Lorenz et al found that CIMT was associated with increased cardiovascular events; CIMT progression over time was not associated with increased cardiovascular event risk. In a systematic review by Peterset al, the added predictive value of CIMT was modest, and the ability to reclassify patients into clinically relevant categories was not demonstrated. The results from these studies and others demonstrate the predictive value of CIMT is uncertain, and the predictive ability for any level of population risk cannot be determined with precision. In addition, available studies do not define how the use of CIMT in clinical practice improves outcomes. There is no scientific literature that directly tests the hypothesis that measurement of CIMT results in improved patient outcomes and no specific guidance on how measurements of CIMT should be incorporated into risk assessment and risk management. The existing evidence is therefore insufficient to determine the impact of this technology on net health outcome.

Practice Guidelines and Position Statements

American College of Cardiology and American Heart Association

A 2013 guideline on the assessment of cardiovascular risk from the American College of Cardiology and the American Heart Association (ACC/AHA) does not recommend CIMT for routine risk assessment of a first atherosclerotic cardiovascular disease event. ACC/AHA Class III: no benefit, LOE: B. This differs from the previous 2010 version of the ACC/AHA guidelines for assessment of cardiovascular risk, which indicated CIMT might be reasonable for assessing cardiovascular risk in intermediate risk asymptomatic adults.

American Society of Echocardiography

The American Society of Echocardiography Consensus Statement endorsed by the Society for Vascular Medicine, states that CIMT is a feature of arterial wall aging "that is not synonymous with atherosclerosis, particularly in the absence of plaque." The statement recommends measurement of both CIMT and carotid plaque by ultrasound "for refining CVD risk assessment in patients at intermediate cardiovascular disease risk (Framingham Risk Score 6–20%) without established CHD, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm." However, the authors acknowledge that, "More research is needed to determine whether improved risk prediction observed with CIMT or carotid plaque imaging translates into improved patient outcomes."

National Cholesterol Education Program Adult Treatment Panel (NCEP ATP)

The Third Report of NCEP ATP does not recommend using "emerging risk factors" in the assessment of persons for primary prevention. It does state that "emerging risk factors" may be useful in certain patient-centered circumstances.

U.S. Preventive Services Task Force Recommendations

In October 2009, the U.S. Preventive Services Task Force (USPSTF) published a systematic review of CIMT within the scope of a larger recommendation statement entitled "Using Nontraditional Risk Factors in Coronary Heart Disease Risk Assessment". On the basis of one fair- and two good-quality studies, the USPSTF states that CIMT, independently of Framingham risk factors, predicts coronary heart disease (CHD) in asymptomatic patients. These studies were longitudinal, population-based studies conducted in the U.S. and the Netherlands. USPSTF reviewed the Atherosclerosis Risk in Communities (ARIC) study and concluded that CIMT measurement can result in risk prediction that is modestly improved, particularly in adult men. However, the review cautions that the studies that did show an association were all done in a research setting, and therefore one cannot draw conclusions on the applicability of CIMT to the intermediate-risk population at large. The studies which USPSTF referenced are further detailed within this policy.

The Summary of Recommendation specific to CIMT is stated as:

> "The U.S. Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of benefits and harms of using…[CIMT]…to screen asymptomatic men and women with no history of CHD to prevent CHD events." The USPSTF identifies the following research need: "The predictive value…of carotid IMT…should be examined in conjunction with traditional Framingham risk factors for predicting CHD events and death."

Key Words:
Carotid intimal medial thickness (CIMT), B-mode ultrasound, intimal medial thickness, IMT, atherosclerosis, ultrasonographic measurement, SonoCalc®, Cardioscan

Approved by Governing Bodies:
In February 2003, SonoCalc® (SonoMetric Health, LLC, Bountiful UT) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this software was substantially equivalent to existing image display products for use in the automatic measurement of the intima media thickness of the carotid artery from images obtained from ultrasound systems. Subsequently, several other devices have been approved through the 510(k) process.

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

Current Coding:
CPT code:

93895	Quantitative carotid intima media thickness and carotid atheroma evaluation, bilateral **(Effective 01/01/15)**
0126T	Carotid intima media thickness

It is possible that providers may incorrectly use the following CPT code:

93880	Duplex scan of extracranial arteries; complete bilateral study

Previous Coding:

93799	Unlisted cardiovascular service or procedure **(Deleted 7/1/15)**

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This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.