Medical Coverage Policy

Effective Date **5/15/2023**
Next Review Date **5/15/2024**
Coverage Policy Number **0475**

Carotid Intima-Media Thickness Measurement

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Related Coverage Resources

Atherosclerotic Cardiovascular Disease Risk Assessment: Emerging Laboratory Evaluations

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses carotid intima-media thickness (CIMT) testing, a noninvasive test where the lining of the carotid arteries is measured with the use of B-mode ultrasound.

Coverage Policy

Coverage of carotid intima-media thickness (CIMT) testing may be governed by state mandates.

Carotid intima-media thickness (CIMT) testing for any indication including the evaluation of atherosclerotic burden or coronary heart disease risk factor assessment is considered experimental, investigational or unproven.

General Background

Measurement of the carotid intima-media thickness (CIMT) is a noninvasive test, where the lining of the carotid arteries is measured with the use of B-mode ultrasound. The intima is the innermost layer of the artery, and the

media is the middle layer of the artery. Carotid ultrasound has been routinely used for evaluation of ischemic cerebrovascular signs and symptoms. In the utilization of carotid ultrasound in the context of risk stratification, the intima-media thickness is measured for the objective of detecting preclinical or subclinical cardiovascular disease. Measurement of the CIMT is considered to be a surrogate marker for the measurement of atherosclerosis, which correlates with the presence of coronary atherosclerosis. This has led to the theory that it may represent an independent marker, separate from the traditional risk factors for cardiovascular disease and stroke. The major independent risk factors are cigarette smoking, elevated blood pressure, elevated serum total and LDL cholesterol, low serum HDL cholesterol, diabetes mellitus, and advancing age. Additional risk factors include obesity, family history of premature coronary heart disease (CHD), and physical inactivity (Pearson, 2002). It is not clear if the measurement of CIMT provides benefit above traditional risk factors or if treatment guided by this test has an effect on clinical outcomes.

The wall thickness can be measured at a single site, such as the far wall of common carotid artery or at several sites including near and far walls of the left and right common carotid arteries, bifurcation, and internal carotid artery (Crouse, 2006). CIMT has been widely used in research as an outcome measurement in studies, including tests involving the following (Simon, et al., 2002):

- testing the value of new or emerging risk factors by means of observational or epidemiological studies in groups of patients or in general populations
- evaluating effects of risk factor modifications by various drugs on progression of early arterial wall alteration in therapeutic trials

Disadvantages that have been identified to be associated with the use of this testing procedure include (Nissen, 2004):

- A high level of technical expertise is needed for precise quantification. In particular, this is needed when the measurement is used in for multicenter studies, since the precision of the studies depends upon the measurement of extremely small differences in thickness.
- There is an incomplete standardization of equipment, with various devices and frequencies employed at different centers.

Difficulties that have been identified with CIMT testing include: poor image quality, drifting, improper machine settings and difficult patient anatomy (e.g., high bifurcations of the carotid artery and deep vessels). At this time, there is a lack of standardization of measurement and imaging protocols. It is not clear whether generalized IMT or focal plaque formation is of more importance. The literature indicates that there are gender- and age-related differences with IMT. A definition of what is considered expected normal limits that take into account these differences has not been established. It is not evident from the literature that CIMT is able to improve on risk prediction above what is provided by utilization of traditional risk factors or the effect of these measurements on patient outcomes.

Literature Review
There is a lack of large population, well-designed studies evaluating the long term health benefits of carotid intima-media thickness (CIMT) testing, including but not limited to for the purpose of risk assessment for an atherosclerotic cardiovascular disease (ASCVD) event. CIMT is used in the clinical research setting to demonstrate the effects of various medications and interventions on carotid intima-media thickness progression.

Systematic reviews: Willeit et al. (2020) conducted a systematic review to quantify the association between effects of interventions on carotid intima-media thickness (cIMT) progression and their effects on cardiovascular disease (CVD) risk. Aims included: quantify the reduction in CVD risk associated with reducing cIMT progression by therapeutic intervention; explore cIMT progression as a surrogate marker for different types of CVD endpoints as well as all-cause mortality; and investigate differences according to the intervention type, method of cIMT assessment, and other trial characteristics. The study included 119 randomized controlled trials (100,667 patients). cIMT was assessed as the mean value at the common-carotid-artery; or if unavailable, the maximum value at the common-carotid-artery or other cIMT measures. The primary outcome was a combined CVD endpoint defined as myocardial infarction, stroke, revascularization procedures, or fatal CVD. Intervention effects on cIMT progression and incident CVD were evaluated for each trial, before relating the two using a Bayesian

meta-regression approach. Over an average follow-up of 3.7 years, 12,038 patients developed the combined CVD endpoint. Across all interventions, each 10 μm/year reduction of cIMT progression resulted in a relative risk for CVD of 0.91 (95% credible interval 0.87-0.94), with an additional relative risk for CVD of 0.92 (0.87-0.97) being achieved independent of cIMT progression. When viewed together, it was estimated that interventions reducing cIMT progression by 10, 20, 30, or 40 μm/year would yield relative risks of 0.84 (0.75-0.93), 0.76 (0.67-0.85), 0.69 (0.59-0.79), or 0.63 (0.52-0.74). Results were similar when grouping trials by type of intervention, time of conduct, time to ultrasound follow-up, availability of individual-participant data, primary vs. secondary prevention trials, type of cIMT measurement, and proportion of female patients. The authors concluded that the effects of interventions on cIMT progression and on CVD risk are associated, endorsing the usefulness of cIMT progression as a surrogate marker in clinical trials

Kumar et al. (2020) conducted a meta-analysis to clarify the association between common carotid artery intima-media thickness (CCA-IMT) with the risk of stroke and its subtype by estimating pooled analysis of published literature. Inclusion criteria were observational studies including case-control, nested case control study, cross-sectional and cohort design investigating the association of CCA-IMT with the risk of stroke and its subtype; imaging confirmed diagnosis of stroke (ischemic or hemorrhagic) using CT or MRI scans; patients aged > 18 years; numbers available for patient and control groups for CCA-IMT values or data provided from which numbers could be calculated. The review included 19 studies, of which sixteen studies involving 3,475 ischemic stroke (IS) cases and 11,826 controls; six studies with 902 large vessel disease (LVD) and 548 small vessel disease (SVD) of IS subtypes; five studies with 228 intracerebral hemorrhage (ICH) and 1,032 IS cases, were included. The findings suggest a strong association between increased CCA-IMT with risk of IS as compared to control subjects [SMD = 1.46, 95% CI = 0.90-2.02]. However it was found that there is an increased risk of LVD as compared to the SVD subtype of IS [SMD = 0.36, 95% CI = 0.19-0.52] and more chance of occurrence of IS rather than ICH [SMD = 0.71, 95% CI = 0.28-1.41]. It was noted that although the analysis was on a large scale, the populations included were mainly from Caucasian; there were fewer studies from Asian population. Carotid intima thickness measurements are found to be associated with the risk of stroke along with its subtypes and that prospective studies embedded with larger sample size are needed to validate the findings in future.

Den Ruijter et al. (2012) conducted a meta-analysis to determine whether common CIMT has added value in 10-year risk prediction of first-time myocardial infarctions or strokes, above that of the Framingham Risk Score. The review included 14 population-based cohorts with data for 45,828 individuals. The studies included participants were drawn from the general population, common CIMT was measured at baseline, and individuals were followed up for first-time myocardial infarction or stroke. Individual data were combined into one data set and an individual participant data meta-analysis was performed on individuals without existing cardiovascular disease. During a median follow-up of 11 years, 4,007 first-time myocardial infarctions or strokes occurred. The risk factors of the Framingham Risk Score were refitted and then the model with common CIMT measurements was extended to estimate the absolute 10-year risks to develop a first-time myocardial infarction or stroke in both models. The added value of common CIMT measurements to the Framingham Risk Score in the general population was found to be minor (0.8% were correctly reclassified). In individuals at intermediate risk, the added value was 3.2% in men and 3.9% in women. The authors concluded that the addition of common CIMT measurements to the Framingham Risk Score was associated with small improvement in 10-year risk prediction of first-time myocardial infarction or stroke, but this improvement is unlikely to be of clinical importance. The findings of this study indicate that there is little clinical utility of using CIMT for cardiac risk assessment.

Lorenz et al. (2012) conducted a meta-analysis to test the association between changes in CIMT and cardiovascular risk (PROG-IMT collaborative project). The review included 16 studies with 36,984 participants. The review identified general population cohort studies that assessed CIMT at least twice and followed up with participants for myocardial infarction, stroke, or death. During a mean follow-up of seven years, 1,519 myocardial infarctions, 1,339 strokes, and 2,028 combined endpoints (myocardial infarction, stroke, vascular death) occurred. Individual participant data meta-analysis was performed. After excluding individuals with previous myocardial infarction or stroke, the association was assessed between CIMT progression and the risk of cardiovascular events (myocardial infarction, stroke, vascular death, or a combination of these) for each study with Cox regression. Yearly CIMT progression was derived from two ultrasound visits 2–7 years apart. No evidence of an association between individual CIMT progression and the risk of subsequent cardiovascular events, irrespective of definition of CIMT, endpoint, and adjustment. The authors strongly advocate further

validations and improvements of ultrasound protocols. The authors concluded that the association between CIMT progression assessed from two ultrasound scans and cardiovascular risk in the general population remains unproven. Further studies are needed to determine how the association between CIMT progression and cardiovascular risk and the assessment of CIMT will affect health outcomes.

Lorenz et al. (2018) conducted a meta-analysis to assess the relation between CIMT change and events in individuals at high cardiovascular risk (results from the PROG-IMT collaboration above). From 31 cohorts with two CIMT scans (n = 89070) on average 3.6 years apart and clinical follow-up, subcohorts were drawn: A) individuals with at least three cardiovascular risk factors without previous CVD events; B) individuals with carotid plaques without previous CVD events; and C) individuals with previous CVD events. Cox regression models were fit to estimate the hazard ratio (HR) of the combined endpoint (myocardial infarction, stroke or vascular death) per standard deviation (SD) of CIMT change, adjusted for CVD risk factors. These HRs were pooled across studies. In groups A, B and C it was observed 3483, 2845 and 1165 endpoint events, respectively. The average common CIMT was 0.79mm (SD 0.16mm), and annual common CIMT change was 0.01mm (SD 0.07mm), both in group A. The pooled HR per SD of annual common CIMT change (0.02 to 0.43mm) was 0.99 (95% confidence interval: 0.95-1.02) in group A, 0.98 (0.93-1.04) in group B, and 0.95 (0.89-1.04) in group C. The HR per SD of common CIMT (average of the first and the second CIMT scan, 0.09 to 0.75mm) was 1.15 (1.07-1.23) in group A, 1.13 (1.05-1.22) in group B, and 1.12 (1.05-1.20) in group C. The authors concluded that although common CIMT is associated with future CVD event risk, this is not apparently true for common CIMT change over time; it is theorized that reasons may include the complexity of atherosclerotic process, and technical limits of current CIMT measurement.

Costanzo et al. (2010) reported on a systematic review conducted with the aim to assess, using a meta-regression analysis of randomized trials whether reduced progression or regression of IMT is associated with a reduced incidence of major cardiovascular events in subjects at intermediate to high cardiovascular risk. The review included 41 trials with 18,307 participants that assessed carotid IMT at baseline, at the end of follow-up, and reporting clinical end points. The influence of baseline patients' characteristics, cardiovascular risk profile, IMT at baseline, follow-up, and quality of the trials was also examined. Although there was a significant reduction in coronary heart disease (CHD) and cerebrovascular (CBV) events, and all-cause death induced by active treatments (for CHD events, odds ratio [OR]: 0.82, 95% confidence interval [CI]: 0.69 to 0.96, p=0.02; for CBV events, OR: 0.71, 95% CI: 0.51 to 1.00, p=0.05; and for all-cause death, OR: 0.71, 95% CI: 0.53 to 0.96, p=0.03), there was no significant relationship between IMT regression and CHD events, CBV events, and all-cause death. It was also noted that subjects' baseline characteristics, cardiovascular risk profile, IMT at baseline, follow-up, and quality of the trials did not significantly influence the association between IMT changes and clinical outcomes. The authors concluded that the regression or slowed progression of CIMT, induced by cardiovascular drug therapies do not reflect reduction in cardiovascular events.

Studies: Polak et al. (2011) conducted a study that examined if the intima–media thickness of the walls of the common carotid artery and internal carotid artery could add to the Framingham risk score for predicting cardiovascular events. The mean intima–media thickness of the common carotid artery and the maximum intima–media thickness of the internal carotid artery were measured in 2,965 members of the Framingham Offspring Study cohort. Cardiovascular disease outcomes were evaluated for an average follow-up of 7.2 years. Multivariable Cox proportional hazards models were generated for intima–media thickness and risk factors. Reclassification was performed of cardiovascular disease on the basis of the 8-year Framingham risk score category (low, intermediate, or high) after adding intima–media thickness values. A total of 296 participants had a cardiovascular event with the risk factors of the Framingham risk score predicting these events , with a C statistic of 0.748 (95% confidence interval [CI], 0.719–0.776). The adjusted hazard ratio for cardiovascular disease with a 1-SD increase in the mean intima–media thickness of the common carotid artery was 1.13 (95% CI, 1.02–1.24), with a nonsignificant change in the C statistic of 0.003 (95% CI, 0.000–0.007); the corresponding hazard ratio for the maximum intima–media thickness of the internal carotid artery was 1.21 (95% CI, 1.13–1.29), with a modest increase in the C statistic of 0.009 (95% CI, 0.003–0.016). The net reclassification index increased significantly after addition of intima–media thickness of the internal carotid artery (7.6%, p<0.001) but not intima–media thickness of the common carotid artery (0.0%, P = 0.99). With the presence of plaque, defined as intima–media thickness of the internal carotid artery of more than 1.5 mm, the net reclassification index was 7.3% (p=0.01), with an increase in the C statistic of 0.014 (95% CI, 0.003–0.025). The authors concluded that the maximum internal and mean common carotid-artery intima–media thicknesses both predict cardiovascular

outcomes, but only the maximum intima–media thickness of (and presence of plaque in) the internal carotid artery had a modest effect of improving the classification of risk of cardiovascular disease in this cohort. Limitations of the study included that the population only included white race and the results may not be applicable to other races or ethnic groups; the follow-up period was 7.2-years up period, which is shorter than the 10-year period for which the Framingham risk score is calculated; and a single experienced and supervised sonographer to was used to obtain high-quality measurements during carotid artery ultrasonography, which may affect the implementation of our findings in primary prevention.

There are several observational, longitudinal studies published that demonstrate a correlation between CIMT measurement and established risk factors for heart disease (Villines, et al., 2017; Geisel, et al., 2017; Nambi, et al., 2010; Kathiresan,, et al., 2007; Amato, et al., 2007; O'Leary, et al., 1999; Hodis, et al., 1998; Bots, et al., 1997; Chambless, et al., 1997).

Although there appears to be an association with established risk factors for heart disease, cohort and case-control studies have not demonstrated that use of this test results in a substantial increase in predictive value when utilized as a screening tool in addition to established risk factors or if patient treatment guided by CIMT improves cardiovascular outcomes (Bot, et al., 2014; Jain, et al., 2011; Folsom et al., 2008; Baldassare, et al., 2007; Kitagawa, et al., 2007; Kanawar, et al., 2007; Gepner, et al., 2006; Iglesias del Sol, et al., 2001).

Professional Societies/Organizations

US Preventive Services Task Force (USPSTF): The 2009 USPSTF Recommendation Statement on Using Nontraditional Risk Factors In Coronary Heart Disease Risk Assessment concluded that the current evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of CHD to prevent CHD events (USPSTF, October 2009). (Grade: I [Insufficient] Statement, current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.) The nontraditional risk factors included in this recommendation are high-sensitivity C-reactive protein (hs-CRP), ankle–brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima–media thickness (carotid IMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine level, and lipoprotein(a) level. (USPSTF, 2009).

The 2018 update to the 2009 USPSTF recommendations does not include carotid IMT. The update concluded that the current evidence is insufficient to assess the balance of benefits and harms of adding the ankle-brachial index (ABI), high-sensitivity C-reactive protein (hsCRP) level, or coronary artery calcium (CAC) score to traditional risk assessment for cardiovascular disease (CVD) in asymptomatic adults to prevent CVD events (USPSTF, 2018).

American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines: The ACC/AHA published updated 2013 ACC/AHA guidelines, in collaboration with National Heart, Lung, and Blood Institute (NHLBI) on the assessment of cardiovascular risk (Goff, et al., 2014). The guidelines include the following regarding CIMT:

- CIMT is NOT recommended for routine measurement in clinical practice for risk assessment for a first Atherosclerotic Cardiovascular Disease (ASCVD) event.

  NHLBI grade: (Grade N*, No Recommendation For or Against)
  ACC/AHA Class III*: No Benefit, LOE B*
  Based on new evidence reviewed during ACC/AHA update of the evidence.

  * Grade N: No recommendation for or against
  There is insufficient evidence or evidence is unclear or conflicting.")
  Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the Work Group thought no recommendation should be made. Further research is recommended in this area.

Class III/LOE B: recommendation that procedure or treatment is not useful/effective and may be harmful; evidence from single randomized trial or nonrandomized studies

American College of Preventive Medicine (ACPM): The ACPM published position statement for atherosclerotic cardiovascular disease screening in adults (Lim, et al., 2011). The statement notes that the ACPM "recommends CHD risk assessment using the FRS [Framingham Risk Score] to guide risk-based therapy. ACPM does not recommend routine screening of the general adult population using electrocardiogram, exercise-stress testing, computed tomography scanning, ankle-brachial index, carotid intima medial thickness, or emerging risk factors, including high-sensitivity C-reactive protein (hs-CRP)."

American Association of Clinical Endocrinologists (AACE): the AACE published updated guidelines for management of dyslipidemia and prevention of cardiovascular disease (Jellinger, et al., 2017). The guidelines include the following recommendation: Carotid intima media thickness (CIMT) may be considered to refine risk stratification to determine the need for more aggressive atherosclerotic cardiovascular disease preventive strategies. (Grade B; best evidence level [BEL] 2).

Use Outside of the US
European Society of Cardiology (ESC): The ESC published updated guidelines on cardiovascular disease prevention in clinical practice. With regard to CIMT the guidelines note that, "The lack of standardization regarding the definition and measurement of IMT, its high variability and low intra-individual reproducibility have raised concerns. A recent meta-analysis failed to demonstrate any added value of IMT compared to the Framingham Risk Score in predicting future CVD, even in the intermediate risk group. Thus, the systematic use of carotid ultrasound IMT to improve risk assessment is not recommended." (Piepoli, et al., 2016)

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD		No Determination found	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
93895	Quantitative carotid intima media thickness and carotid atheroma evaluation, bilateral

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