



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Carotid Intima-Media Thickness Measurement

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Coverage Policy

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

CIGNA does not cover carotid intima-media thickness (CIMT) testing for any indication including the evaluation of atherosclerotic burden or coronary heart disease risk factor assessment because it 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, 2000). 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 and Levenson, 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) (Mitchell, et al., 2004). 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 (Mancini, et al., 2004). 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 have been several systematic reviews published that examine the role of CIMT measurements in cardiac risk assessment. A systematic evidence synthesis of nine novel risk factors for CHD, including CIMT, for intermediate-risk persons was conducted for the US Preventive Services Task Force (USPSTF) (Helfand, et al., 2009). Regarding CIMT, the review noted that:

- Six population-based longitudinal studies (five cohorts) in asymptomatic persons followed for the development of CHD
- The reports from two of the five studies had no adjustment for other risk factors and were rated poor-quality
- CIMT persisted as an independent risk factor in the three cohorts after full or partial adjustment for Framingham risk factors. The relative risks or hazard ratios ranged from 1.19–3.80 for various degrees of CIMT (mm) or a composite score of CIMT or plaque.
- No data was identified regarding the prevalence of high CIMT among asymptomatic intermediate-risk individuals
- Regarding future research recommendations it was noted, "Epidemiologic cohorts that have measured carotid IMT should measure the impact of carotid IMT on prediction of CHD events among intermediate-risk individuals and on reclassification of these individuals. It is highly plausible that intervention directed toward modification of traditional risk factors in individuals with increased carotid IMT might reduce the risk of subsequent CHD. Randomized controlled trials are needed to evaluate this hypothesis."

Wald et al. (2009) reported on a meta-analysis of studies that assessed the screening performance of CIMT and carotid plaque in identification of individuals with CHD. The review included 18 case-control and cohort studies that involved 2,920 individuals with CHD and 41,941 without. An assessment of screening performance (detection rates [DRs] for specified false positive rates [FPRs]) was carried out from the relative Gaussian distributions of IMT among individuals with and without CHD and from the proportion of affected and unaffected

individuals with plaque. Findings included: for plaque that the DR was 62% for an FPR of 30%; and for IMT, the DR was 65% for the same 30% FPR. The authors concluded that neither carotid plaque nor IMT has a CHD screening performance that is sufficiently discriminatory between affected and unaffected individuals to be considered a worthwhile screening test.

Baldassarre et al. (2008) conducted a meta-analysis of 107 studies addressing the association between CIMT and soluble markers and to investigate whether these observed inconsistencies could be explained by the characteristics of the patients included in different studies (e.g., the prevalence of atherosclerotic disease, gender, age, or occurrence of specific vascular risk factors [VRFs]). Regardless of the marked heterogeneity of results presented in the literature, the meta-analysis demonstrated that studies showing positive associations between CIMT and plasma levels of C-reactive protein (CRP) or fibrinogen are in the majority. The data regarding the relationships between CIMT and other soluble markers are by contrast noted to be scanty, contradictory, or unconfirmed by multivariate (as opposed to univariate) analyses, and the freedom from publication bias here cannot be assured. Gender, noninsulin-dependent diabetes mellitus (NIDDM) and hypercholesterolemia appeared to influence the association between CIMT and CRP. Blood pressure and hypercholesterolemia appeared to influence the association between CIMT and fibrinogen. The heterogeneity in ultrasound methodologies and in statistical approach limited comparability between studies.

Lorenz et al. (2007) conducted a systematic review of the literature to provide an overview of the relevant studies, critically appraise the methods used and, where possible, to perform a meta-analysis to gain more robust estimates of the predictive value of increased IMT to predict future clinical cardiovascular end points. The review included eight observational studies with general population based samples for which CIMT was measured and follow-up for clinical end points were provided. The studies represented 37,197 subjects followed for a mean of 5.5 years. Major sources of heterogeneity were age distribution, carotid segment definition and IMT measurement protocol. The review found that CIMT is a strong predictor of future vascular events. In addition, it was noted that the relative risk per IMT difference is slightly higher for the end point of stroke than for MI. The review also noted heterogeneity between the studies regarding the details of the ultrasound protocols. These details included: the precise definitions of the carotid segments investigated, the use of mean or maximal IMT, the measurement of near and far wall or IMT, and whether IMT is measured on one side or both sides. It is recommended that in future studies of IMT, ultrasound protocols should be aligned with published studies. It appears that data for younger individuals is limited, and additional studies are required.

There are several observational, longitudinal studies published that demonstrate a correlation between CIMT measurement and established risk factors for heart disease (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 is an association with established risk factors, 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 (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).

Lorenz, et al. (2010) published results of a ten-year follow-up of a cohort of 4,904 patients without pre-existing vascular disease in the Carotid Atherosclerosis Progression Study (CAPS). The usefulness of CIMT in individual risk prediction beyond the Framingham and the SCORE models was investigated. The authors found that while CIMT was predictive for cardiovascular endpoints, it did not consistently improve the risk classification of individuals.

Professional Societies/Organizations

American College of Cardiology: The 34th Bethesda Conference, sponsored by the American College of Cardiology Foundation, was held in 2002 for the topic: Can Atherosclerosis Imaging Techniques Improve the Detection of Patients at Risk for Ischemic Heart Disease? The purpose of the conference was to review the current status and controversies within the integration of atherosclerosis imaging into clinical cardiovascular medicine. The report noted that additional testing, such as imaging, must provide incremental risk-prediction information to the Framingham Risk Score. In discussing the emerging techniques for noninvasive measurement of atherosclerosis, including measurement of CIMT, it is noted that "None of the available tests have yet been demonstrated to impact CHD management or outcomes." Task Force 3 reviewed the existing and emerging noninvasive technologies for atherosclerosis imaging. The task force noted that different protocols and standardization are used by different laboratories, and it is difficult to establish normal and abnormal values

adjusted for gender and age. In addition, they noted that “None of these imaging technologies have been shown to make prevention more effective, although their integration into office-based risk factor assessment is under active study.” With regard to CIMT, they noted that (Redberg et al., 2003):

- Carotid ultrasonography can produce measurements for plaque or IMT; studies that have clearly distinguished IMT from plaque demonstrate that CHD risk is largely associated with the presence of nonobstructive or obstructive plaque rather than IMT.
- The current data available supports the use of this test mainly in middle-aged and older patients.

American Diabetes Association and American College of Cardiology Foundation: A consensus statement from these two organizations was published regarding lipoprotein management in patients with cardiometabolic risk (Brunzell, et al., 2008). The report included the following statements regarding CIMT measurement:

- The presence of so-called subclinical vascular disease may be determined by measuring coronary calcification, carotid intima-media thickness, or the ankle-brachial index. Patients with documented subclinical atherosclerosis are at increased cardiovascular disease risk and may be considered candidates for more aggressive therapy
- Whether such tests improve prediction or clinical decision making in patients with diabetes or cardiometabolic risk is unclear.

American Heart Association (AHA): The AHA-sponsored Prevention Conference V: Beyond Secondary Prevention: Identifying the High-Risk Patient for Primary Prevention. Writing Group III, considered noninvasive tests of atherosclerotic burden. Regarding measurement of CIMT, the following was noted (Smith, et al., 2000):

- Cross-sectional associations between common carotid artery IMT and cardiovascular risk factors have been demonstrated in several studies.
- At least four published studies found that CIMT measurement was a viable predictor of the presence of coronary atherosclerosis and its clinical outcomes; thus, this test is an independent risk factor for coronary heart disease events and strokes.
- They concluded that in asymptomatic individuals older than 45 years of age, carefully performed carotid ultrasound examination with IMT measurement can add incremental information to traditional risk factor assessment and can be considered for further clarification of CHD assessment at the request of a physician.

American Society of Echocardiography (ASE) American and the Society of Vascular Medicine and Biology: A report published in 2006 by these two organizations, Clinical Application of Noninvasive Vascular Ultrasound in Cardiovascular Risk Stratification, notes that numerous carotid artery imaging protocols have been proposed. The protocols and methodological aspects are reviewed in the report. The report notes that protocols may vary in the number of segments in which IMT is measured, whether the near wall is measured in addition to the far wall, and whether IMT measurements are derived from B-mode or M-mode ultrasound images (Roman, et al., 2006).

In 2008, these two organizations published a consensus statement—Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force Endorsed by the Society for Vascular Medicine (Stein, et al., 2008). In order to address the issues of standardization and assist in improving the availability of experienced clinical laboratories that can perform high-quality CIMT studies, the societies have provided recommendations for carotid ultrasound scanning protocol. It is noted that since a randomized controlled trial studying the effectiveness of carotid ultrasound imaging as a tool to modify preventive therapies and improve cardiovascular disease outcomes has not been performed, the clinical practice recommendations are based on observational data. The guidelines note that additional research is required in order to determine whether improved risk prediction observed with CIMT or carotid plaque imaging translates into improved patient outcomes. The recommendations for performing CIMT include:

- Measuring CIMT and identifying carotid plaque by ultrasound are most useful for refining cardiovascular risk assessment in patients at intermediate cardiovascular risk (i.e., Framingham risk score 6-20% without established coronary heart disease, peripheral arterial disease, cerebrovascular disease, diabetes mellitus or abdominal aortic aneurysm).
- CIMT assessment and carotid plaque detection may also be considered in the following situations:
 - patients with family history of premature cardiovascular disease in a first degree relative (i.e., men <55 years old, women <65 years old)

- individuals younger than 60 years old with severe abnormalities in a single risk factor (e.g., genetic dyslipidemia) who otherwise would not be candidates for pharmacotherapy
- women younger than 60 years old with at least two cardiovascular risk factors
- Imaging should not be performed in the following situations:
 - with established atherosclerotic vascular disease
 - if the results would not be expected to alter therapy
- Serial studies of CIMT to address progression or regression are not recommended.

Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council Cardiovascular Radiology and Intervention, American Heart Association:

A consensus statement from these groups was published regarding the role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease (Mieres, et al., 2005). The consensus statement makes the following notations regarding CIMT:

- CIMT is one of several emerging imaging modalities in the detection of subclinical atherosclerotic heart disease in women that has not amassed the wealth of evidence that would clearly define the role in the clinical evaluation of women with suspected atherosclerotic heart disease.
- The advantages of CIMT include the wide availability of ultrasound technology, absence of ionizing radiation or incidental scan findings and well-validated nature of the test results.
- The limitations of the test include the lack of accepted technical standards for IMT testing and the absence of published population distributions of IMT. Further precise documentation of what defines an abnormal level of IMT and measurement guidelines are needed.
- The clinical use of CIMT for risk stratification in asymptomatic women has not been shown to result in improved outcomes.

European Society of Cardiology (ESC): The ESC published the European guidelines on cardiovascular disease prevention in clinical practice. With regard to CIMT the guidelines note that (De Backer, et al., 2003; Graham, et al., 2007):

- CIMT is an independent predictor of cerebral and coronary events but seems to be more predictive in women than in men.
- Carotid ultrasound can add information beyond assessment with traditional risk factors which may help to make decisions about the necessity to institute medical treatment for primary prevention.
- One limitation of using carotid ultrasound for global risk assessment is the absence of reliable data relating IMT numbers to ten-year event rates.
- It is not currently clear how IMT measurements can be formally incorporated into existing risk algorithms used in asymptomatic persons.

Mannheim Carotid Intima-Media Thickness Consensus (2004-2006): The Mannheim Consensus was convened to standardize methods used in the measurement of CIMT. The consensus statement notes that, "Although IMT has been suggested to represent an important risk marker, according to the current evidence it does not fulfill the characteristics of an accepted risk factor. Standardized methods recommended in this consensus statement will foster homogenous data collection and analysis. This will help to improve the power of randomized clinical trials incorporating IMT measurements and to facilitate the merging of large databases for meta-analyses." It is noted that there is no need to "treat IMT values nor to monitor IMT values in individual patients." (Touboul, et al., 2007)

National Heart, Lung and Blood Institute (NHLBI): The NHLBI sponsored the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (ATP III) (National Institutes of Health [NIH], 2002). The ATP III report, in the section regarding tests for atherosclerotic plaque burden, notes the following regarding CIMT:

- The extent of carotid atherosclerosis correlates positively with the severity of coronary atherosclerosis
- Recent studies show that severity of IMT independently correlates with risk for major coronary events
- Measurement of CIMT theoretically could be used as an adjunct in CHC risk assessment.
- Its expense, lack of availability and difficulties with standardization preclude a current recommendation for its use in routine risk assessment for the purpose of modifying intensity of LDL-lowering therapy.

US Preventive Services Task Force (USPSTF): The 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)

Summary

Carotid intima-media thickness (CIMT) measurement is a noninvasive test that serves as a surrogate marker for coronary atherosclerosis. There is a correlation between CIMT and traditional coronary risk factors. The clinical utility of measuring IMT for the purpose of predicting risk of coronary or cerebral events 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.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
0126T	Common carotid intima-media thickness (IMT) study for evaluation of atherosclerotic burden or coronary heart disease risk factor assessment

ICD-9-CM Diagnosis Codes	Description
	All codes

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	3/15/2008	0475	Carotid Intima-Media Thickness Measurement

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