Medical Policy

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

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DESCRIPTION

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.

Background

Coronary heart disease (CHD) accounts for 27% of all deaths in the U.S. (1) Established major risk factors for CHD have been identified by the National Cholesterol Education

Program Expert Panel (NCEP). 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 use of the Framingham criteria to further stratify those patients with 2 or more risk factors for more intensive lipid management. (2) 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 measurement of the carotid intima-medial thickness (CIMT) has been investigated as a technique to identify and monitor subclinical atherosclerosis. B-mode ultrasound is most commonly used to measure CIMT. The intima-medial thickness (IMT) 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 2 lines constitutes the IMT.

Regulatory Status

In February 2003, SonoCalc® (SonoMetric Health, LLC, Bountiful, UT) was cleared for marketing by the U.S. Food and Drug Administration (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 IMT of the carotid artery from images obtained from ultrasound systems. Subsequently, several other devices have been approved through the 510(k) process.

POLICY

Ultrasonographic measurement of carotid artery intimal-medial thickness (CIMT) as a technique of identifying subclinical atherosclerosis is considered **experimental / investigational** for use in the screening, diagnosis, or management of atherosclerotic disease.

RATIONALE

The most recent literature search was performed for the period May 2011 through May 2012. A summary of the key literature follows.

Evaluation of a diagnostic technology typically focuses on the following 3 parameters: 1) technical performance; 2) diagnostic parameters (sensitivity, specificity, positive and negative predictive value); and 3) demonstration of clinical utility; the diagnostic information can be used to improve patient outcomes.

Literature Review

The literature on the use of carotid intima-media thickness (IMT) 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.

Diagnostic Utility

Systematic reviews. In a 2012 meta-analysis of individual participant data pooled from 16 studies with a total of 36,984 patients, Lorenz and colleagues examined carotid intima-medial thickness (CIMT) progression from 2 ultrasound screenings taken 2-7 years apart (median 4 years). (3) Patients were followed for a mean of 7 years during which time 1,339 strokes, 1,519 myocardial infarctions (MI) and 2,028 combined endpoints (MI, stroke, vascular death) occurred. The mean CIMT of the 2 ultrasounds results was predictive of cardiovascular risk using the combined endpoint (adjusted hazard ratio [HR]: 1.16, 95% confidence interval [CI]: 1.10-1.22). In sensitivity analyses, no associations were found between cardiovascular risk and individual CIMT progression regardless of CIMT definition, endpoint, and adjustments. As an example, for the combined endpoints, an increase of one standard deviation (SD) in mean common CIMT progression resulted in an overall estimated HR of 0.97 (95% CI: 0.94-1.00) when adjusted for age, sex, and mean common CIMT, and HR was 0.98 (0.95-1.01) 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 a 2012 systematic review of subclinical atherosclerosis imaging techniques, Peters et al. reviewed 12 studies on CIMT that examined reclassification of risk. (4) For the impact on the primary outcome of cardiovascular events, when CIMT was added to the prediction model, the range of increase in the c-statistic was 0.00 to 0.03 on a scale of 0-1.0. Net reclassification improvement with CIMT was reported in 5 of the studies included in the review and ranged from -1.4% to 12%.

Recent studies have found including carotid plaques in CIMT increases the predictive value of cardiovascular risk over CIMT assessed only in plaque-free sites. (5-8) 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. (3) The systematic review by Peters found adding carotid plaque to the traditional CIMT model increased the c-statistic from 0.01 to 0.06. (4) In 2010, Mookadam and colleagues conducted a systematic review of the role of CIMT in predicting individual cardiovascular event risk and as a tool in assessing therapeutic interventions. (9) 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.

Prospective cohort studies. In the Atherosclerosis Risk in Communities (ARIC) study, the authors evaluated risk factors associated with increased CIMT in 15,800 subjects. (10) 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 4 to 7 years of follow-up. (11) 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 CHD risk factors but remained elevated for higher measurements of CIMT. The authors concluded that mean CIMT is a noninvasive predictor of future coronary heart disease (CHD) incidence.

The Rotterdam study was a prospective cohort study that started in 1989 and recruited 7,983 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 individuals. 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 myocardial infarction (MI). (12) O'Leary and colleagues performed CIMT in 4,476 asymptomatic subjects aged 65 years or older without clinical cardiovascular disease. (13) 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 4,904 subjects. All subjects received a baseline CIMT measurement, as well as traditional risk factor analysis, and were followed over a 10-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. (14) 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 5 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.

Several other studies have, in fact, used CIMT measurements as outcome measures. In this setting, serial measurements of CIMT are performed, as opposed to a single measure. For example, the Asymptomatic Carotid Artery Progression Study (ACAPS) was designed to evaluate the role of lovastatin (an HMG-CoA reductase inhibitor, i.e., a statin drug) in patients asymptomatic for cardiovascular disease and with low-density lipoprotein (LDL) cholesterol levels

at or below the limits established by the National Cholesterol Education Program. (15, 16) A total of 919 asymptomatic men and women were randomly assigned to receive various combinations of lovastatin, warfarin, and placebo over a 3-year period. The principal outcome measurement was the progression of CIMT, tested at 6 sites in both carotid arteries. Lovastatin treatment was associated with a reduction in the progression of mean maximum CIMT. The Monitored Atherosclerosis Regression Study also included measurements of CIMT every 6 months for 4 years in a subset of enrolled subjects. (17) The authors concluded that lipid-lowering therapy resulted in a regression of CIMT.

CIMT is frequently being used in the research setting but application or widespread use is uncertain. In the Multi-Ethnic Study of Atherosclerosis (MESA) trial, an ongoing cohort study of atherosclerosis, (18) 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 6,698 adults asymptomatic at baseline. In a 2010 article from MESA, CIMT results in 4,792 healthy, nondiabetic adults who were not on lipid-lowering medications were compared in 6 different lipid groups, including normolipemia and several types of common dyslipidemias. (19) 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 6,760 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. (20) In the Bogalusa Heart Study of 991 subjects, obesity along with overweight and elevated metabolic risk were also associated with increased CIMT. (21) 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 1,254 subjects. (22) CIMT is also used as a surrogate outcome measure in atherosclerosis treatment research studies. (23)

In 2010, Raiko et al. compared cardiovascular disease risk-scoring tools for identification of CHD risk to CIMT results in 2,204 healthy adults, aged 24-39 years, from the Cardiovascular Risk in Young Finns study. (24) 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 6 years later.

Conclusions. 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 and colleagues, 355 patients, aged 40 years with one or more cardiovascular disease risk factor, received carotid ultrasound screenings to prospectively determine whether abnormal results would change physician and patient behaviors. (25) 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= .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. Since 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.

Conclusions. 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.

Ongoing Trials

A search of the online site ClinicalTrials.gov database in June 2012 identified one open, randomized, controlled trial. The IMPRESS Study (NCT01330602) will randomly stratify 1,310 subjects with an intermediate risk of cardiovascular events and a family history of premature atherosclerosis to either a disease management program with intensive pharmacologic and behavioral interventions for primary prevention or usual health care management. The study will evaluate whether the disease management program is effective and whether changes in CIMT over 3 years can determine atherosclerotic status and future cardiovascular events.

Summary

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 2 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.

Some studies correlate increased CIMT with many other commonly used markers for risk of CHD and with risk for future cardiovascular events. While 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 Peters and colleagues, (4) 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 appears to be no scientific literature that directly and experimentally 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 data are insufficient to determine the impact of this technology on net

health outcome. Therefore, CIMT is considered investigational for use in the screening, diagnosis, or management of atherosclerotic disease.

Practice Guidelines and Position Statements

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". (26) On the basis of one fair- and 2 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."

The 2010 American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines (27) indicate: "Measurement of carotid artery IMT is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk." The guidelines note an increased CIMT reading may be used as a guide in determining clinical treatment, but evidence has not demonstrated improvements in outcomes when incorporating CIMT measurement into treatment decision making. Additionally, the Guidelines state: "Clinical tools integrating carotid IMT within global risk scoring systems are not available. The incremental value of carotid IMT and cost effectiveness beyond that available from standard risk assessments to improve overall patient outcomes is not established." Furthermore, "serial scanning of carotid IMT is challenging in individual patients across brief time horizons due to variability in measurement in relation to the rate of disease progression and is therefore not recommended in clinical settings."

The American Society of Echocardiography Consensus Statement (28) 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."

The ATP III 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. (2)

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

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

- In January 1, 2006, a CPT category III code specific to this test was added: 0126T.
- It is possible that providers might incorrectly use CPT code 93880, which describes bilateral duplex scan of extracranial arteries.

DIAGNOSIS

Experimental / investigational for all diagnoses related to this policy.

REVISIONS

08-24-2009	Policy added to the bcbsks.com web site.
09-06-2011	Description section updated
	Rationale section updated
	In Coding section ▪ Added the instructional phrase "It is possible that providers might incorrectly use CPT code 93880, which describes bilateral duplex scan of extracranial arteries."
	References updated
09-18-2012	Description section updated
	Rationale section updated
	References updated

REFERENCES

1. Minino AM, Heron MP, Murphy SL et al. Deaths: final data for 2004. Natl Vital Stat Rep 2007; 55(19):1-119.
2. Pasternak RC. Report of the Adult Treatment Panel III: the 2001 National Cholesterol Education Program guidelines on the detection, evaluation and treatment of elevated cholesterol in adults. Cardiol Clin 2003; 21(3):393-8.
3. Lorenz MW, Polak JF, Kavousi M et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet 2012; 379(9831):2053-62.

4. Peters SA, den Ruijter HM, Bots ML et al. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart 2012; 98(3):177-84.
5. Plichart M, Celermajer DS, Zureik M et al. Carotid intima-media thickness in plaque-free site, carotid plaques and coronary heart disease risk prediction in older adults. The Three-City Study. Atherosclerosis 2011; 219(2):917-24.
6. Keo HH, Baumgartner I, Hirsch AT et al. Carotid plaque and intima-media thickness and the incidence of ischemic events in patients with atherosclerotic vascular disease. Vasc Med 2011; 16(5):323-30.
7. Nambi V, Chambless L, He M et al. Common carotid artery intima-media thickness is as good as carotid intima-media thickness of all carotid artery segments in improving prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. Eur Heart J 2012; 33(2):183-90.
8. Xie W, Liang L, Zhao L et al. Combination of carotid intima-media thickness and plaque for better predicting risk of ischaemic cardiovascular events. Heart 2011; 97(16):1326-31.
9. Mookadam F, Moustafa SE, Lester SJ et al. Subclinical atherosclerosis: evolving role of carotid intima-media thickness. Prev Cardiol 2010; 13(4):186-97.
10. Dobs AS, Nieto FJ, Szklo M et al. Risk factors for popliteal and carotid wall thicknesses in the Atherosclerosis Risk in Communities (ARIC) Study. Am J Epidemiol 1999; 150(10):1055-67.
11. Chambless LE, Heiss G, Folsom AR et al. Association of coronary heart disease incidence with carotid arterial wall thickness and major risk factors: the Atherosclerosis Risk in Communities (ARIC) Study, 1987-1993. Am J Epidemiol 1997; 146(6):483-94.
12. van der Meer IM, Bots ML, Hofman A et al. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. Circulation 2004; 109(9):1089-94.
13. O'Leary DH, Polak JF, Kronmal RA et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999; 340(1):14-22.
14. Lorenz MW, Schaefer C, Steinmetz H et al. Is carotid intima media thickness useful for individual prediction of cardiovascular risk? Ten-year results from the Carotid Atherosclerosis Progression Study (CAPS). Eur Heart J 2010; 31(16):2041-8.
15. Probstfield JL, Margitic SE, Byington RP et al. Results of the primary outcome measure and clinical events from the Asymptomatic Carotid Artery Progression Study. Am J Cardiol 1995; 76(9):47C-53C.
16. Byington RP, Evans GW, Espeland MA et al. Effects of lovastatin and warfarin on early carotid atherosclerosis: sex-specific analyses. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group. Circulation 1999; 100(3):e14-7.
17. Hodis HN, Mack WJ, LaBree L et al. Reduction in carotid arterial wall thickness using lovastatin and dietary therapy: a randomized controlled clinical trial. Ann Intern Med 1996; 124(6):548-56.
18. Folsom AR, Kronmal RA, Detrano RC et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). Arch Intern Med 2008; 168(12):1333-9.
19. Paramsothy P, Knopp RH, Bertoni AG et al. Association of combinations of lipid parameters with carotid intima-media thickness and coronary artery calcium in the MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 2010; 56(13):1034-41.

20. Blaha MJ, Rivera JJ, Budoff MJ et al. Association between obesity, high-sensitivity C-reactive protein ≥2 mg/L, and subclinical atherosclerosis: implications of JUPITER from the Multi-Ethnic Study of Atherosclerosis. Arterioscler Thromb Vasc Biol 2011; 31(6):1430-8.
21. Camhi SM, Katzmarzyk PT, Broyles ST et al. Subclinical atherosclerosis and metabolic risk: role of body mass index and waist circumference. Metab Syndr Relat Disord 2011; 9(2):119-25.
22. Green D, Foiles N, Chan C et al. An association between clotting factor VII and carotid intima-media thickness: the CARDIA study. Stroke 2010; 41(7):1417-22.
23. Bots ML, Palmer MK, Dogan S et al. Intensive lipid lowering may reduce progression of carotid atherosclerosis within 12 months of treatment: the METEOR study. J Intern Med 2009; 265(6):698-707.
24. Raiko JR, Magnussen CG, Kivimaki M et al. Cardiovascular risk scores in the prediction of subclinical atherosclerosis in young adults: evidence from the cardiovascular risk in a young Finns study. Eur J Cardiovasc Prev Rehabil 2010; 17(5):549-55.
25. Johnson HM, Turke TL, Grossklaus M et al. Effects of an office-based carotid ultrasound screening intervention. J Am Soc Echocardiogr 2011; 24(7):738-47.
26. Using nontraditional risk factors in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2009; 151(7):474-82.
27. Greenland P, Alpert JS, Beller GA et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2010; 56(25):e50-103.
28. Stein JH, Korcarz CE, Hurst RT et al. 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. J Am Soc Echocardiogr 2008; 21(2):93-111; quiz 89-90.