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Coronary Computed Tomography Angiography for Screening of an Asymptomatic Population: Too Much or Too Soon?

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Atherosclerotic cardiovascular disease is a global health problem. Many published statistics have shown correspondence of a large disease burden with the economic burden attributed to atherosclerotic cardiovascular disease. Better identification of asymptomatic individuals at high risk for coronary artery disease (CAD) to receive aggressive risk reduction therapy is an important challenge for the primary prevention of cardiovascular disease. CAD is known to involve a prolonged asymptomatic phase. Frequently, the first clinical presentation of CAD results in serious morbidity or mortality, and approximately 50% of all acute coronary syndromes (ACS) occur in previously asymptomatic subjects.¹⁾ In addition, despite the etiologic importance in atherosclerosis, cardiovascular risk factors have been shown to poorly predict asymptomatic subjects of the risks of developing CAD.²⁾

Recently, sophisticated imaging technology has been developed and several imaging modalities are used as good screening tools to identify patients at high risk for cardiovascular disease. Commonly used non-invasive atherosclerosis imaging techniques in the clinical setting include carotid intima-media thickness and plaque measured by ultrasound; coronary artery calcium as detected by cardiac computed tomography; ankle-brachial index as measured by distal pressure Dop-

pler measurement; and the aortic pulse wave velocity as measured by carotid and femoral pressure wave recordings with a Doppler or mechanographic device.³⁾ Simon et al.⁴⁾ compared the prognostic performance of subclinical atherosclerosis tests in predicting CAD in asymptomatic individuals. Positive testing for subclinical atherosclerosis is associated with a moderately high to high CAD risk. However, different types of subclinical atherosclerosis tests differ in their prognostic performances. It is recognized that a "detection gap" exists, defined as the difference between CAD cases or events currently detected and the total burden of disease or events among the population.⁵⁾

Multi-slice coronary computed tomography angiography (CCTA) has emerged as a very attractive, non-invasive diagnostic modality to visualize the coronary arteries, including the location, severity, and characteristics of atherosclerotic plaque.⁶⁾ Because CCTA comprehensively evaluates the composition (calcific and non-calcific) of coronary plaques, CCTA may provide prognostic evidence independent of, and incremental to, CT calcium scoring. CCTA can assess the presence of subclinical atherosclerosis and may be a useful tool for early CAD detection in asymptomatic subjects.

Although many studies have demonstrated the diagnostic or prognostic value of CCTA in significant CAD, such studies in asymptomatic subjects are limited.⁷⁻⁹⁾ Choi et al.⁷⁾ assessed the value of CCTA as a screening tool for the detection of occult CAD in 1,000 asymptomatic Korean subjects. Specifically, 22% of individuals had detectable coronary atherosclerosis, but only 5% had significant stenoses. Coronary events occurred in individuals with detectable plaques, but most of them were revascularizations triggered by the fact that an atherosclerotic lesion had been detected. Similarly, although a 26-36% prevalence of significant CAD was detected in asymptomatic type 2 diabetic patients,^{8,9)} the prognostic value of these observations are uncertain due to a lack of follow-up. Moreover, the precise role of CCTA in the diagnostic work-

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up of patients, even those with suspected CAD in relation to existing non-invasive functional tests (electrocardiogram-stress test, stress-single photon emission CT, or dobutamine echocardiography), has not been established.

In a recent review, Lee et al.¹⁰⁾ also assessed the role of CCTA in identifying subclinical CAD in 4,320 asymptomatic Korean individuals. It seemed to be an extension of a previous study⁷⁾ with a larger population at the same institute. They showed similar results, that coronary artery plaques were present in 24% of individuals and significant CAD was identified in only 3% of subjects. While it was encouraging that a challenging study with a large population was conducted in Korea, several limitations and concerns were raised in this study. First, because there were no confirmative data in CAD and no follow-up data, they could not prove a definite role for CCTA in risk stratification or prognosis. Second, there existed patient bias. Although they were referred for general health evaluation, only 20% of patients underwent CCTA for further cardiac evaluation for clinical reasons. Specifically, in men, more than 50% belonged to the moderate- and high-risk groups. Detection of significant CAD may have been lower if CCTA was performed blindly in an asymptomatic population. Third, they did not perform multivariate analysis for CAD, including age, gender, and various co-morbidities, and it was therefore difficult to define an independent or additive role for CCTA in risk stratification of CAD.

In addition, when considering the current use of CCTA for risk stratification in asymptomatic individuals, injection of the mandatory contrast agent and exposing patients to substantially higher radiation doses compared to coronary calcium measurements must be taken into account. The American College of Cardiology recently endorsed a list of appropriate uses for CCTA. Specifically, CCTA is currently not recommended for risk stratification and screening in asymptomatic populations, due to lack of favorable prognostic data in asymptomatic individuals.¹¹⁾

It is still debated whether and how subclinical atherosclerosis should be treated. Recently, statin therapy has been shown to delay the progression of atherosclerosis in clinical studies.¹²⁾ In the Multi-Ethnic Study of Atherosclerosis (MESA)¹³⁾ among adults with high coronary calcium scores, 95% remained asymptomatic over the subsequent 5 years, and most people with abnormal findings on screening will remain disease free. Another concern is that asymptomatic healthy subjects may turn into "patients" with occult coronary atherosclerosis, which may trigger anxiety and result in further diagnostic procedures and unnecessary treatment.

Taylor et al.⁵⁾ reported on atherosclerosis imaging techniques and the detection of patients at risk of ischemic heart disease at the Bethesda Conference 34. They concluded that a valuable screening test should have the following character-

istics: 1) identify both high- and low-risk groups accurately; 2) enhance the identification of high-risk individuals, 3) result in a favorable impact on disease outcomes; 4) be relatively risk free; 5) be cost-effective when compared to the current screening modalities; and 6) educate the public concerning atherosclerosis and vascular disease risk.

In conclusion, before embracing CCTA as a routine screening procedure, the potential benefits of screening must be shown to outweigh the potential harmful effects, and further studies supporting a correlation between plaque progression imaging and future cardiovascular events are needed.

REFERENCES

- 1) Murabito JM, Evans JC, Larson MG, Levy D. Prognosis after the onset of coronary heart disease: an investigation of differences in outcome between the sexes according to initial coronary disease presentation. *Circulation* 1993;88:2548-55.
- 2) Khot UN, Khot MB, Bajzer CT, et al. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003;290:898-904.
- 3) Simon A, Levenson J. May subclinical arterial disease help to better detect and treat high-risk asymptomatic individuals? *J Hypertens* 2005;23:1939-45.
- 4) Simon A, Chironi G, Levenson J. Comparative performance of subclinical atherosclerosis tests in predicting coronary heart disease in asymptomatic individuals. *Eur Heart J* 2007;28:2967-71.
- 5) Taylor AJ, Merz CN, Udelson JE. 34th Bethesda Conference: executive summary-can atherosclerosis imaging techniques improve the detection of patients at risk for ischemic heart disease? *J Am Coll Cardiol* 2003;41:1860-2.
- 6) Achenbach S. Computed tomography coronary angiography. *J Am Coll Cardiol* 2006;48:1919-28.
- 7) Choi EK, Choi SI, Rivera JJ, et al. Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. *J Am Coll Cardiol* 2008;52:357-65.
- 8) Romeo F, Leo R, Clementi F, et al. Multislice computed tomography in an asymptomatic high risk population. *Am J Cardiol* 2007;99:325-8.
- 9) Rivera JJ, Nasir K, Choi EK, et al. Detection of occult coronary artery disease in asymptomatic individuals with diabetes mellitus using non-invasive cardiac angiography. *Atherosclerosis* 2009;203:442-8.
- 10) Lee S, Choi EK, Chang HJ, et al. Subclinical coronary artery disease as detected by coronary computed tomography angiography in an asymptomatic population. *Korean Circ J* 2010;40:434-441.
- 11) Hendel RC, Patel MR, Kramer CM, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *J Am Coll Cardiol* 2006;48:1475-97.
- 12) Santos RD, Nasir K. Insights into atherosclerosis from invasive and non-invasive imaging studies: should we treat subclinical atherosclerosis? *Atherosclerosis* 2009;205:349-56.
- 13) Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008;358:1336-45.