OHTAC Recommendation

Multidetector Computed Tomography for Coronary Artery Disease Screening in Asymptomatic Populations

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**Issue Background**

Coronary artery disease (CAD) is the leading cause of death in the western world. Occlusion of coronary arteries reduces coronary blood flow and oxygen delivery to the myocardium. The rupture of an unstable atherosclerotic plaque may result in myocardial infarction. If left untreated, coronary heart disease can result in heart failure, and death. According to the Heart and Stroke Foundation of Canada, 54% of all cardiovascular deaths are due to CAD. Almost half of cases of CHD have no prior symptoms and occur without warning.

Recently, the Association for the Eradication of Heart Attack in the United States (US) released its Screening for Heart Attack Prevention and Education (SHAPE) practice guidelines, calling for noninvasive screening to detect sub-clinical atherosclerosis in asymptomatic men aged 45 years to 75 years, and asymptomatic women aged 55 years to 75 years who are not considered very low risk. It was estimated that the above target populations include approximately 50 million people in the US. Based on the population of Ontario, this translates to approximately 1.9 million people in this province. Proposed screening methods for detecting asymptomatic coronary artery calcification include the use of electron beam computed tomography (EBCT) or multi-detector computed tomography (CT). Some experts in Ontario are recommending the use of 64 slice CT angiography for diagnosing CAD in asymptomatic high risk patients.

Coronary calcification has been observed in all stages of atherosclerotic plaque development, and is, therefore, considered a surrogate marker of CAD. Within coronary vessels, the quantity of coronary calcium correlates moderately closely with the extent of atherosclerotic plaque burden whereas the presence or absence of calcium is not closely associated with the propensity of an individual atherosclerotic plaque to rupture. It has been suggested that an asymptomatic person’s coronary calcium score can be integrated with other risk factors for risk stratification and goal-directed prevention. Computed tomography (CT), is a medical imaging method employing tomography to generate a three-dimensional image taken around a single axis of rotation. Contrast-enhanced MSCT is performed for noninvasive imaging of the coronary arteries. Computer software quantifies the amount of calcium within the coronary arteries and calculates coronary artery calcium score (CAC). Compared to conventional CT scanning, MSCT can provide smaller pieces of information and can cover a larger area faster. Advanced MSCT technology (8, 16, 32, and 64-slice systems) is capable of producing more images in less time. For general CT scanning, this faster capability can reduce how long people are required to be still during the procedure and thereby reduce potential movement artefact. MSCT angiography is being proposed as a minimally invasive replacement for coronary angiography (CA) to diagnose CAD. There are several multi-slice CT systems licensed as class 3 medical devices. One EBCT was licensed by Health Canada as a class III medical device; however the license was discontinued in October 2005. As EBCT is not currently licensed in Canada, it is beyond the scope of this review. Alternative methods of assessing CAD include patient history and physical examination, electrocardiogram, exercise stress test, SPECT, echocardiography, coronary angiography, intravascular ultrasound (IVUS), and MRI.

**OHTAC Findings**

From the literature search, 7 studies were relevant to the MAS review. There were 6 systematic reviews on the effectiveness of CT screening for asymptomatic populations, 4 observational studies examining
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MSCT screening for CAD in asymptomatic populations, and 1 RCT and 2 prospective cohort studies on the impact of screening on behaviour modification retrieved from the literature review that met the inclusion and exclusion criteria.

MSCT screening of asymptomatic individuals, does not currently meet the WHO criteria, and hence is not justifiable. Issues not addressed to meet the WHO criteria include defining a target population, particularly with regards to risk stratification as a precursor to screening, CAC cut-offs for referral to further testing and treatment, and absence of RCTs on screening program effectiveness. Additional ethical questions raised include the risks and benefits of screening, and safety issues regarding screening programs.

Two studies found a positive association of the presence of CAC predictive of future cardiovascular events included frequency, severity, and survival. MSCT exhibits moderately high sensitivity (86%) and moderate specificity (69%) for detection of CAD in an asymptomatic population. Implications of population based screening if it were to occur would include a high rate of false positives and result in increased downstream costs and interventions without evidence of effectiveness. Additionally, some cases of CAD will be missed. Cardiovascular risk factors are positively associated with the presence of CAC and cardiovascular events; however risk factor stratification to identify high risk asymptomatic individuals is unclear with the current evidence-base.

No studies have addressed whether the addition of CT to measure CAC changes patient management of individuals in comparison to standard risk assessment. However, 3 studies examined the impact of EBCT screening on patient motivation to change or modify risk factor related behavior, including smoking, diet, and physical activity levels. Only the number of risk factors, physician led-interventions, and intensive case management were associated with reduction or stabilization of risk factors, with the exception of smoking-related behaviour. Knowledge of CAC score was not found to modify patient behaviour. General CT scanning poses a risk of radiation exposure. Patient radiation exposure is not regulated, nor have specific radiation level exposure limits been established for patients undergoing diagnostic procedures. CT examination could have up to 400 times more radiation than a plain film chest x-ray. The risk of cancer associated with an individual CT scan is 1 in 1000. There is a potential linear dose relationship with CT radiation. Safety of MSCT screening is also an issue because of the introduction of increased radiation doses for initial screening scan and possible follow-up interventions. No studies examining the cost effectiveness of MSCT screening for CAD in asymptomatic populations were located. No Ontario based costs-analysis was performed for MSCT screening for CAD in asymptomatic patients and there was insufficient evidence to determine clinical effectiveness and justify screening.

OHTAC found a lack of evidence of benefit of screening asymptomatic populations with limited low-quality evidence of effectiveness, radiation safety risks, and the potential burden on the health care system.

The evidence suggests that CAC levels are predictive of future coronary events. However, due to the clinical performance of MSCT, many false positives requiring subsequent additional diagnostic work-up may occur and there would also be a proportion of individuals with CAC who would not be detected on initial scan. MSCT screening for CAD does not meet the WHO criteria for screening, and radiation doses
may be unacceptable to patients. There was no evidence to suggest that MSCT screening for CAD results in changes of management of these individuals, and there was no evidence from a RCT to indicate that screening, case management, and knowledge of CAC scores modifies lifestyle cardiovascular factors. There was evidence that knowledge of CAC score also does not alter smoking habits. The sensitivity and specificity of CT for CAC compared to IVUS among CAD asymptomatic patients referred for PCI (Van Miegham, 2006) were: Sensitivity 86% (95% CI 74-93%) and Specificity 69% (95% CI 44-86%).

There is no evidence from the literature review on long-term downstream consequences on the effect of screening. Additionally, there are no studies that examine treatment of CAD based on CAC scores in asymptomatic people. Addressing safety the reviewer reported that: patient radiation dose is not monitored or legislated in Ontario, the lifetime cancer risk ~1/1000 for each scan, typical CT exam could have up to 400 time more radiation than a plain film chest x-ray, there is a potential linear dose effect, and a careful examination of scanning parameters should be undertaken (OHTAC & UHN Factors Usability Lab Report).

The review concluded that the technology did not meet WHO criteria for screening and that the downstream outcomes were unknown. Also, current evidence for screening effectiveness in predicting risk for CAD was of low to very-low quality, there were radiation safety issues, there was no evidence on cost or change in patient management, and generalizability of some studies to asymptomatic populations may be inappropriate.

**OHTAC Recommendations**

Based on the above findings, OHTAC recommends:

No population based screening is recommended. The utility of Multi-slice CT angiography for screening for CAD in asymptomatic patients has not been established.