Washington State Health Care Authority

Health Technology Assessment

Peer Review and Public Comments & Responses

Coronary Artery Calcium Scoring (CACS) as a Diagnostic Test for Detection of Coronary Artery Disease

Date: Wednesday, September 9th, 2009

Health Technology Assessment Program
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SPECTRUM RESEARCH RESPONSE TO PEER REVIEW COMMENTS

Note 1: Spectrum is an independent vendor contracted to produce evidence assessment reports for WA HTA program. For transparency, all comments received during the comments process are included. However, comments related to program decisions, process, or other matters not pertaining to the report are acknowledged through inclusion, but are not within the scope of response for report accuracy and completeness.

Note 2: Individuals who provided peer review on the published public draft (when it was published online) are listed in Appendix I. This role should not be construed to mean that the individuals were authors or primary contributors to the formulation of the draft, nor does it imply endorsement, approval, or disapproval of the process or report.

1. Noel S. Weiss, MD, DrPH, Professor, Epidemiology University of Washington

Dr. Weiss' comment on CACS as a means of reducing use of angiography, SRI response
Additional clarification of this context was made where appropriate.

Dr. Weiss' comment on CACS >0 and sensitivity, SRI response
Clarification was made where appropriate.

Dr. Weiss' comment on safety, SRI response
Context regarding the potential for decreased radiation exposure if CACS reduces the use of angiography was added.

Dr. Weiss' comment on benefits of CACS in the absence of a comparison group, SRI response
Text describing test features which may allow for estimation of CACS benefit in the absence of a comparison group has been added.

Dr. Weiss' comment on risk for fatal cancer, SRI response
This has been corrected.

2. Rita F. Redberg, MD, MSc, UCSF Division of Cardiology, Professor of Clinical Medicine

Dr. Redberg's comment on general overview, pre-test probability of disease, SRI response
Additional context was added to reflect the comments and some wording changes were made in appropriate places.

Dr. Redberg's comments on the background, SRI response
Additional context was added regarding ischemia in patients with no CAC. The terminology related to exercise treadmill testing was corrected.

The California Technology Assessment Forum (CTAF), report recommendations state that:

> As a diagnostic test in patients with symptoms suggestive of CAD does not meet technology assessment criteria 3, 4, or 5 for safety, effectiveness, and improvement in health outcomes.

Based on clarification of data and testimony from invited experts, the CTAF panel accepted the following recommendation:

> As a diagnostic test in patients with symptoms suggestive of CAD (i.e. chest pain) EBCT calcium scoring was determined to be a useful technology in the prediction of those patients who will have underlying coronary disease.

This additional context has been added to the report.

Dr. Redberg's comment on additional testing and radiation exposure, SRI response
Context regarding the potential for decreased radiation exposure if CACS could reduce the use of angiography was added as was some context regarding the potential for increased exposure in persons who have positive CACS and require further testing.

Dr. Redberg's comment on economic evaluation, SRI response
Additional context regarding the need to consider the impact of additional testing has been added where appropriate.

3. Ann Derleth, PhD, MSPH, Health Services Researcher, Health Economics Research Associate- University of Washington

Dr. Derleth's comment on public policy, SRI response
SRI is an independent vendor contracted to provide assessment of the scientific evidence on the technologies and does not suggest policy. The report is evaluated by the State's Health Technology Clinical Committee, whose responsibility it is to discuss and suggest policy.

SPECTRUM RESEARCH RESPONSE TO PUBLIC COMMENTS

Spectrum is an independent vendor contracted to produce evidence assessment reports for WA HTA program. For transparency, all comments received during the comments process are included. However, comments related to program decisions, process, or other matters not pertaining to the report are acknowledged through inclusion, but are not within the scope of response for report accuracy and completeness.

Response to professional society comments

SCCT comment regarding page 5, number 2 (radiation safety), SRI response
The lower bound of 0.7mSv from the AHA document has been added to the ranges reported in this HTA. Table 1 of Gerber reports the "Representative Effective Dose value (mSV)" for CACS as 3 mSV, with a footnote which indicates that the estimate reflects a combination of prospective and retrospective gating. That Writing Group estimates 1mSV for prospective gating, which is within the range reported in this HTA. It is good to know that the majority of testing currently employs prospective gating and other ways of decreasing radiation exposure. Information on methods for decreasing radiation exposure is reflected in the background portion of the report and summary of professional guidelines.

SCCT comment regarding page 6, number 2 (incidental findings), SRI response
The study by O'Malley is among asymptomatic patients and did not meet inclusion criteria. While this trial in population of relatively young active duty military personnel did not show increased stress or anxiety, an earlier observational study on a larger, less select population of asymptomatic persons by Wong, et al, did report that increased worry was significantly associated with test results. Since it was in an asymptomatic population, it did not meet inclusion criteria. It is logical to consider that follow-up of incidental findings has the potential to increase worry as well as cost and inconvenience related to additional testing.

SCCT comment regarding page 9, SRI response
The AHA Scientific Statement is included in the background together with other relevant guidelines.

SCCT comment regarding coverage, SRI response
By contract, SRI is required to provide information on any CMS National Coverage Decision (NCD) and policies from two bell-weather payers. The United Health Care policy described was published after the search dates.

The relevant local CMS coverage decision is for Region X (Alaska, Oregon, Washington), LCD ID number L23654, which states:

> Demonstration and/or quantification of the presence of coronary calcification in either asymptomatic or symptomatic patients with or without signs of atherosclerotic heart disease has not been shown to improve outcomes and is not covered. Until such time as there may be more evidence of medical necessity, Medicare will not pay for the quantitative evaluation of coronary calcium by MDCT, CTCA, EBCT or other technology.

SCCT comment regarding asymptomatic persons, SRI response
SRI is an independent vendor contracted to provide assessment of technologies based on questions determined by the State Technology Assessment Program.

UNIVERSITY OF WASHINGTON

DEPARTMENT OF EPIDEMIOLOGY
School of Public Health and Community Medicine

To: Andrea C. Skelly, PhD, MPH
Epidemiologist
Spectrum Research, Inc.

From: Noel S. Weiss, MD, DrPH NSW
Professor

Re: Peer review for the Calcium Scoring HTA

At your request, I'm providing my assessment of the document you prepared, Coronary Artery Calcium Scoring as a Diagnostic Test for Detection of Coronary Artery Disease. Though you provided me with an evaluation form, I am not using it because the categories listed on the form do not correspond to those present in your document. I hope that my comments will prove helpful even if they do not follow the specific format indicated.

Overall, I believe the report thoroughly and accurately addressed the question posed to you, i.e. the potential role of coronary artery calcium scoring as a means of detecting coronary artery disease in symptomatic persons. Your effort to identify relevant studies was comprehensive, the criteria you used to include specific studies for analysis were appropriate, and the summary of the findings of those studies was accurate. The data extracted from the studies were nicely displayed, and the conclusions arrived at on the basis of those data were reasonable ones.

I believe there are several small errors in the report, and several instances in which the material has not been presented as clearly as possible. Here are my suggested modifications:

A. In the Executive Summary, under Summary and Implications (page 5), I recommend that the context in which CACS is being considered should be re-emphasized. That is, CACS is being evaluated as a possible means of reducing the use of coronary angiography. The interpretation of the positive and negative predictive values will be facilitated by having that clinical context clearly specified.

B. In the same section (as well as several times later in the document), I believe the sensitivity of 99% (for a CACS greater than 0) indicates that

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the test is highly sensitive for identifying the presence of obstructive CAD, not for "ruling out" this condition.

C. In the Executive Summary and later in the report, I believe the issue of safety, as it applies to the radiation dose received as part of the evaluation of CAC, is not relevant given the purpose of this evaluation. Rather, what is of concern is the size of the reduced radiation exposure associated with CAC evaluation as opposed to routine coronary angiography. It is not being proposed that a CAC be obtained in addition to angiography. Rather, the question is whether CAC measurement might replace angiography in some patients.

D. On page 7 of the Executive Summary, in the section on clinical decision making and patient outcomes, the lack of a "comparison group", is noted. I agree that to directly address the clinical utility of CAC evaluation, a very large study could be considered that would compare health outcomes between one group of symptomatic patients receiving CAC evaluation first, and angiography only in patients having a CACS score above a certain level, and a group in whom angiography is uniformly provided. However, even in the absence of such a comparison, I believe that it is possible to assess the potential benefit of CACS in clinical decision making. Specifically, if CACS were a perfectly sensitive test, and there were no false negatives, then if with any specificity at all, the benefit of performing a CAC evaluation first could be estimated without having an explicit basis for comparison.

E. On page 53, in the first full paragraph, first sentence, there is a misstatement. That sentence reads, "In the U.S., one in five people are at risk for fatal cancer." The fact is that all people in the U.S. are at risk for fatal cancer. Rather, approximately one in five people will die from cancer.

The above concerns notwithstanding, I would rate the overall quality of this report as "Superior".

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Reviewer Name Rita F. Redberg

INTRODUCTION Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Overview of topic is adequate?
- Topic of assessment is important to address?
- Public policy and clinical relevance are well defined?

Overview of topic is excellent. The topic is important, although I think CACS is used much more commonly in asx persons than in sx persons.

GENERAL OVERVIEW POINTS TO CONSIDER
In general it is important to remember that CACS is an anatomic test. Current ACC/AHA guidelines say that a noninvasive test for ischemia should be done before proceeding tor revascularization, this test would almost always be a stress test, which is a functional test. CACS will never replace functional testing, as it does not detect ischemia. And CACS will never replace coronary angiography, which is the gold standard anatomic test. In addition, a "positive CACS" often leads to additional testing, such as a stress test and/or coronary angiography.

Pretest probability of disease
The accuracy of a test is related to the prevalence of disease in the population studied. For CAD, pre-test probability is largely determined by age, sex and type of chest pain symptoms (Diamond and Forrester 1979 NEJM).

I would not say . The symptoms of CAD have poor specificity and sensitivity for CAD,--- this statement depends on age, sex and symptoms. For example, a 55 year old man with classic angina has a 95% chance of having CAD. It is in patients with low pre test likelihood of CAD that the symptoms are less helpful, such as younger patients, and women.

BACKGROUND Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Content of literature review/background is sufficient?

I would add an article by Schenker (Circulation 2008) which looked at 695 persons with intermediate risk using CACS and PET and showed that the frequency of ischemia among patients with no CAC was 16.0%,

CACS is often followed by a stress test.
Also an exercise treadmill test is abbreviated ETT , ECG means electrocardiogram.
Jeff Tice's assessment for CTAF found that CACS did NOT meet criteria .

REPORT OBJECTIVES & KEY QUESTIONS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Aims/objectives clearly address relevant policy and clinical issue?
- Key questions clearly defined and adequate for achieving aims?

METHODS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Method for identifying relevant studies is adequate?

- Criteria for the inclusion and exclusion of studies is appropriate?
- Method for Level of Evidence (LoE) rating is appropriate and clearly explained?
- Data abstraction and analysis/review are adequate?

RESULTS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Amount of detail presented in the results section appropriate?
- Key questions are answered?
- Figures, tables and appendices clear and easy to read?
- Implications of the major findings clearly stated?
- Have gaps in the literature been dealt with adequately?
- Recommendations address limitations of literature?

CONCLUSIONS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Are the conclusions reached valid?

OVERALL PRESENTATION and RELEVANCE Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Is the review well structured and organized? YES
- Are the main points clearly presented? YES
- Is it relevant to clinical medicine?
- Is it important for public policy or public health? YES

I would add when considering cost of CACS compared to other alternative strategies, one must consider that a positive CACS frequently leads to another test, such as a stress test or coronary angiogram. This is because CACS is anatomic and not a definitive anatomic test, such as angio, and because it is not totally trusted to not have another test which is better known and studied, such as an exrcise test. This practice effects the cost-effectiveness, radiation exposure and overall risk/benefit.

QUALITY OF REPORT

Quality Of the Report (Click in the gray box to make your selection)
Superior XX☐this is an excellent report summarizing a lot of information on a challenging topic. A great contribution and clearly a lot of work.
Good ☐
Fair ☐
Poor ☐

Reviewer Name Ann M Derleth, PhD, MSPH

INTRODUCTION Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Overview of topic is adequate?
- Topic of assessment is important to address?
- Public policy and clinical relevance are well defined?

COMMENTS:
Overview, background, questions and clinical considerations are presented clearly. It is important to address what role CACS offers in the diagnosis of coronary artery disease in relation to existing tests.

Page 10, Line 12-15; Public policy is implied here and throughout the section, but could it be stated more directly?

BACKGROUND Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Content of literature review/background is sufficient?

COMMENTS:
The background is sequenced well and clear.

REPORT OBJECTIVES & KEY QUESTIONS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Aims/objectives clearly address relevant policy and clinical issue?
- Key questions clearly defined and adequate for achieving aims?

COMMENTS:
Aims /objectives are clear.
Key questions clear and adequate.

METHODS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Method for identifying relevant studies is adequate?
- Criteria for the inclusion and exclusion of studies is appropriate?
- Method for Level of Evidence (LoE) rating is appropriate and clearly explained?
- Data abstraction and analysis/review are adequate?

COMMENTS:
Methods, criteria, rating and abstraction /review process all clearly explained and well done.

RESULTS Comments

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Amount of detail presented in the results section appropriate? yes
- Key questions are answered? yes
- Figures, tables and appendices clear and easy to read?
- Implications of the major findings clearly stated?

- Have gaps in the literature been dealt with adequately? Yes
- Recommendations address limitations of literature? Yes – careful consideration was given to limitations throughout.

COMMENTS:
See after questions above – no comments requiring response.

CONCLUSIONS Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:

- Are the conclusions reached valid? Yes

OVERALL PRESENTATION and RELEVANCE Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:

- Is the review well structured and organized? Yes
- Are the main points clearly presented? yes
- Is it relevant to clinical medicine? Very relevant
- Is it important for public policy or public health? Yes .

QUALITY OF REPORT

Quality Of the Report (Click in the gray box to make your selection)
Superior ☐**x**
Good ☐
Fair ☐
Poor ☐

Society of Cardiovascular Computed Tomography
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August 24, 2009

To: Washington State Health Care Authority

RE: Health Technology Assessment Draft Report -- Coronary Artery Calcium Scoring (CACS) as a Diagnostic Test for the Detection of Coronary Artery Disease

To Whom It May Concern:
On behalf of the Society of Cardiovascular Computed Tomography (SCCT), the international professional society representing physicians, scientists and technologists advocating for research, education and clinical excellence in the use of cardiovascular computed tomography, I am writing to express our concerns regarding the findings of the Washington State Technology Assessment's draft report on coronary artery calcium scoring.
SCCT believes the lack of an assessment of CAC testing in asymptomatic persons is an important oversight, and some of the conclusions/assertions regarding CAC testing in symptomatic persons require adjustment based on specific comments we have provided for your consideration (see below). Use of CAC testing in symptomatic persons should be a covered service, as it leads to a significant reduction in invasive testing (Habert 2001).
Specifically, we call your attention to the following:
Page 5, Number 2 - The radiation dose estimates are higher than published from the American Heart Association scientific statement (Budoff, Circulation 2006), and virtually all published studies of calcium scoring. The AHA Scientific Statement on Cardiac CT (Budoff et al, circulation 2006) estimated the radiation exposure of calcium scoring to be 0.7 mSev for Electron Beam Computed Tomography (EBCT) and 1.2 mSev for calcium scoring with MDCT (prospective imaging, which was the recommended, and most commonly used, protocol). Over 90% of all calcium scores are prospectively gated, using data from ICACTL and published studies (over 1000 calcium scoring studies have been published in peer review literature; the vast majority [well over 80%] are done prospectively). The Gerber paper (Circulation 2009) reported dose estimates of 1 mSev for calcium scoring using prospective triggering, not 3 mSev as quoted. Background radiation in the United States is 3-7 mSev per year, so 1 mSev scan done once has never been shown to have any impact on the cancer risk of the population.

Page 6, Number 2 - Quotes "The follow-up of less serious findings may create patient anxiety in addition to exposing them to the inconvenience, costs and risks of additional testing." The only randomized trial of CAC Testing vs. no CAC testing looked at anxiety and found no increased anxiety with test results (O'Malley PG, Feuerstein IM, Taylor AJ. Impact of electron beam tomography, with or without case management, on motivation, behavioral change, and cardiovascular risk profile: a randomized controlled trial. JAMA 2003; 289:2215–23).

Page 9 – The conclusion "From a public health perspective, a diagnostic test should only be performed if it leads to the use of interventions that, on average, are likely to improve patient outcomes or if it prevents the use of interventions that are not likely to improve outcomes." This supports the use of CAC testing in symptomatic persons, as a negative test in symptomatic persons has a 99% negative predictive value in multiple studies (Budoff, AHA Scientific Statement Circulation 2006). This would imply, and has been shown, with up to 7 year follow-up, demonstrating that cardiac catheterization can be safely avoided with a negative calcium score, thus fulfilling the requirement that this test "prevents the use of interventions that are not likely to improve outcomes."

This is consistent with the data on page 21 "A negative test (score = 0) makes the presence of atherosclerotic plaque, including unstable or vulnerable plaque, highly unlikely.

• A negative test makes the presence of significant luminal obstructive disease highly unlikely.

• A negative test is consistent with a low risk (0.1% per year) of a cardiovascular event in the next 2 to 5 years."

Coverage – Local Coverage Decisions for Medicare now cover calcium scoring for symptomatic persons in 9 states. No mention of these positive coverage decisions was listed on Table 3. Furthermore, United Health Care now provides national coverage (Policy Date 7.1.09), for calcium scoring. Interestingly, this was the only major provider not included in the table.

The most important and best validated utility of CAC is use of risk stratification in intermediate risk asymptomatic persons, and this was not covered in the analysis.

Thank you for the opportunity to provide these public comments.

Sincerely,

Matthew Budoff, MD
President-elect
Society of Cardiovascular Computed Tomography