Potential Implications of Coronary Artery Calcium Testing for Guiding Aspirin Use Among Asymptomatic Individuals With Diabetes

Michael Gordon Silverman, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease
Michael J. Blaha, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease
Matthew J. Budoff, Harbor UCLA
Juan J. Rivera, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease
Paolo Raggi, Emory University
Leslee J Shaw, Emory University
Daniel Berman, Cedars-Sinai Medical Center
Tracy Callister, Tennessee Heart and Vascular Center
John A. Rumberger, Princeton Longevity Center
Jamal S. Rana, Cedars-Sinai Medical Center

Only first 10 authors above; see publication for full author list.

Journal Title: Diabetes Care
Volume: Volume 35, Number 3
Publisher: American Diabetes Association | 2012-03-01, Pages 624-626
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.2337/dc11-1773
Permanent URL: https://pid.emory.edu/ark:/25593/s5ns8

Final published version: http://dx.doi.org/10.2337/dc11-1773

Copyright information:
© 2012 by the American Diabetes Association.
This is an Open Access work distributed under the terms of the Creative Commons Attribution-NonCommerical-NoDerivs 3.0 Unported License (http://creativecommons.org/licenses/by-nc-nd/3.0/).

Accessed April 17, 2019 7:21 AM EDT
Potential Implications of Coronary Artery Calcium Testing for Guiding Aspirin Use Among Asymptomatic Individuals With Diabetes

Michael Gordon Silverman, MD1
Michael J. Blaha, MD, MPH1
Matthew J. BuDoff, MD2
Juan J. Rivera, MD, MPH3
Paolo Raggi, MD3
Leslie J. Shaw, PhD3

Daniel Berman, MD4
Tracy Callister, MD4
John A. Rumberger, MD, PhD6
Jamal S. Rana, MD, PhD4
Roger S. Blumenthal, MD1
Khurram Nasir, MD, MPH1,7

OBJECTIVE—It is unclear whether coronary artery calcium (CAC) is effective for risk stratifying patients with diabetes in whom treatment decisions are uncertain.

RESEARCH DESIGN AND METHODS—Of 44,052 asymptomatic individuals referred for CAC testing, we studied 2,384 individuals with diabetes. Subjects were followed for a mean of 5.6 ± 2.6 years for the end point of all-cause mortality.

RESULTS—There were 162 deaths (6.8%) in the population. CAC was a strong predictor of mortality across age-groups (age <50, 50–59, ≥60), sex, and risk factor burden (0 vs. ≥1 additional risk factor). In individuals without a clear indication for aspirin per current guidelines, CAC stratified risk, identifying patients above and below the 10% risk threshold of presumed aspirin benefit.

CONCLUSIONS—CAC can help risk stratify individuals with diabetes and may aid in selection of patients who may benefit from therapies such as low-dose aspirin for primary prevention.

Diabetes Care 35:624–626, 2012

Although diabetes has been considered a coronary heart disease (CHD) risk equivalent (1), not all individuals with diabetes carry equivalent risk. Coronary artery calcium (CAC), a marker of atherosclerosis, has been shown to independently predict cardiovascular events as well as enhance risk stratification in patients with diabetes (2–5). Although recent guidelines recommend consideration of CAC testing for risk assessment in adults with diabetes ≥40 years (6), we sought to evaluate whether CAC effectively stratifies individuals with diabetes across age, sex, and risk factor (RF) burden. This question is particularly important given recent guidelines recommending selected use of aspirin in patients with diabetes based on underlying CHD risk (7).

RESEARCH DESIGN AND METHODS—The study cohort consisted of 44,052 asymptomatic individuals without known CHD referred for CAC screening. There were 2,384 (5.4%) individuals with diabetes by self-report. Details for RF collection have been described previously (8). All subjects underwent CAC scoring at baseline and were followed for a mean of 5.6 ± 2.6 years (median 5 years, range 1 to 13 years) for the primary end point of all-cause mortality verified using the Social Security Death Index. Annualized all-cause mortality rates were estimated by dividing number of deaths by number of person-years at risk.

The population was stratified into the following age-groups: <50, 50–59, and ≥60 years. Additionally, individuals were stratified into high-, intermediate-, and low-risk subgroups (based on age/sex and presence of additional RF) per recent guidelines detailing aspirin use in patients with diabetes as follows: I) high risk (10-year cardiovascular disease [CVD] risk >10%: ‘aspirin is reasonable’): men ≥50 and women ≥60 with 1 or more RF; 2) intermediate risk (10-year CVD risk 5–10%: ‘aspirin might be considered’): men ≥50 and women ≥60 without RF and men <50 and women <60 with RF; and 3) low risk (10-year CVD risk <5%: ‘aspirin should not be recommended’): men <50 and women <60 without RF (7).

RESULTS—Mean age of the 2,384 study subjects was 58 ± 11 years; 52% were men. A total of 500 participants (21%) were <50 years old, 863 (36%) were age 50–59, and 1,021 (43%) were at least 60 years old. A total of 533 individuals (22%) had CAC = 0, whereas 779 (33%) and 1,070 (45%) had CAC 1–100 and >100, respectively. Overall, there were 162 deaths (6.8%). CAC was a strong predictor of mortality in each age-group (expressed in deaths/1,000 person-years with 95% CI): age <50, CAC 0: 0; CAC 1–100: 7.8 (3.7–16.3); CAC >100: 18.2 (9.1–36.4); age 50–59, CAC 0: 3.2 (1–10.1); CAC 1–100: 7.3 (3.9–13.5); CAC >100: 16.6 (11.1–24.7); and age ≥60, CAC 0: 9.9 (4.4–22); CAC 1–100: 19.2 (12.5–29.5); CAC >100: 33.1 (26.7–41).

Notably, all individuals ≥60 years with ≥1 RF had a mortality rate >10 deaths/1,000 person-years.

Table 1 presents mortality rates by CAC score according to estimated 10-year CVD

From the 1Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, Maryland; the 2Los Angeles Biomedical Research Institute at Harbor-UCLA, Torrance, California; the 3Division of Cardiology, Emory University, Atlanta, Georgia; the 4Department of Imaging and Medicine, Cedars-Sinai Medical Center, Los Angeles, California; the 5Tennessee Heart and Vascular Center, Hendersonville, Tennessee; the 6Princeton Longevity Center, Princeton, New Jersey; and the 7Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University, New Haven, Connecticut.

Corresponding author: Khurram Nasir, knasir1@jhmi.edu.

Received 12 September 2011 and accepted 21 November 2011.

DOI: 10.2337/dc11-1773

© 2012 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons.org/licenses/by-nc-nd/3.0/ for details.
Table 1—All-cause mortality rates by CAC score according to estimated 10-year CVD risk per the recent aspirin use guidelines* (based on age, sex, and presence of RFs)

<table>
<thead>
<tr>
<th>Predicted 10-year CVD risk per guidelines</th>
<th>Number of individuals (%)</th>
<th>Number of deaths (%)</th>
<th>Mortality rate/1,000 person-years at risk</th>
<th>95% CI for rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (&lt;5%) “aspirin not recommended”</td>
<td>89</td>
<td>38 (42.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CAC = 0</td>
<td></td>
<td>35 (39.3)</td>
<td>1 (2.9)</td>
<td>5.75</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td></td>
<td>16 (18)</td>
<td>3 (18.8)</td>
<td>39.42</td>
</tr>
<tr>
<td>Intermediate risk (5–10%)</td>
<td>“aspirin to be considered”</td>
<td>979</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAC = 0</td>
<td></td>
<td>288 (29.4)</td>
<td>3 (1)</td>
<td>2.29</td>
</tr>
<tr>
<td>CAC 1–100</td>
<td></td>
<td>370 (37.8)</td>
<td>10 (2.7)</td>
<td>6.24</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td></td>
<td>321 (32.8)</td>
<td>27 (8.4)</td>
<td>20.37</td>
</tr>
<tr>
<td>High risk (&gt;10%)</td>
<td>“aspirin reasonable”</td>
<td>1,316</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAC = 0</td>
<td></td>
<td>209 (15.9)</td>
<td>6 (2.9)</td>
<td>6.59</td>
</tr>
<tr>
<td>CAC 1–100</td>
<td></td>
<td>374 (28.4)</td>
<td>26 (7)</td>
<td>16.32</td>
</tr>
<tr>
<td>CAC &gt;100</td>
<td></td>
<td>733 (55.7)</td>
<td>86 (11.7)</td>
<td>28.60</td>
</tr>
</tbody>
</table>

*Risk classification according to recent guidelines for aspirin use in patients with diabetes (7): 1) high risk (10-year CVD risk >10%: ‘aspirin is reasonable’): men ≥50 and women ≥60 with 1 or more RF; 2) intermediate risk (10-year CVD risk 5–10%: ‘aspirin might be considered’): men ≥50 and women ≥60 without RF and men <50 and women <60 with RF; and 3) low risk (10-year CVD risk <5%: ‘aspirin should not be recommended’): men <50 and women <60 without RF.

CONCLUSIONS—We have shown that CAC measurements may help risk stratify patients with diabetes across age-group, sex, and RF burden. Most individuals with diabetes <60 years of age have a low near-term risk of <5 deaths/1,000 person-years when CAC = 0. Additionally, we have shown that most individuals with CAC >100 have a mortality rate of >10 deaths/1,000 person-years. We have also demonstrated that individuals with diabetes ≥60 years have a mortality rate of >10 deaths/1,000 person-years, regardless of CAC score, when at least one other RF is present.

Although diabetes is defined by some guidelines as a CHD risk equivalent, the use of aspirin for primary prevention among individuals with diabetes remains controversial. Given the conflicting data, a consensus group recently provided updated recommendations concluding that patients with diabetes with a 10-year CVD risk >10% should receive low-dose aspirin for primary prevention (7), further emphasizing the importance of enhanced risk stratification among individuals with diabetes.

CAC has the potential to identify individuals who are at higher risk and thus might benefit from aspirin (based on a 10-year CVD risk >10%) and who may not otherwise be identified by age and RF-based risk estimates. Additionally, among individuals identified as high risk by age and RF (10-year CVD risk >10% and thus recommended for aspirin), 16% had CAC = 0, which translated into a mortality rate of <10 deaths/1,000 person-years; this suggests that even among individuals classified as high risk by age and RF, absence of CAC can identify individuals with a 10-year CVD risk <10%, whose risk of bleeding from aspirin may outweigh potential benefit.

The main limitation of our data is the use of all-cause mortality in place of CVD event rates. Although most deaths in patients with diabetes are cardiovascular in origin, many CVD events do not result in death. This would predominantly lead to number rate underestimation. Self-reported RF is an additional limitation. Although the absence of continuous risk variables may represent an additional limitation, the use of categorical RF data has been validated as a method of risk stratification (9).

In conclusion, CAC has the ability to help risk stratify individuals with diabetes across age-group, sex, and RF burden and may help identify individuals who may benefit from more aggressive therapy, such as low-dose aspirin, for primary prevention. Our study also points to individuals with diabetes who likely will not benefit from CAC testing, namely those ≥60 years with additional RF, because their 10-year CVD risk is >10%. Although our study is informative, definitive recommendations must come from clinical outcomes trials where treatment decisions are driven by CAC-based risk stratification.

Acknowledgments—This research was conducted without dedicated funding. M.J. Bu. is on the speaker’s bureau for General Electric. No other potential conflicts of interest relevant to this article were reported.

M.G.S. and M.J. Bla. were involved in all steps of this study/article. M.J. Bu., J.J.R., P.R., L.J.S., D.B., T.C., J.A.R., J.S.R., and R.S.B. were involved in study planning, data interpretation, abstract editing, and article editing. K.N. was involved in all steps of this study/article and is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

5. Agarwal S, Morgan T, Herrington DM, et al. Coronary calcium score and prediction of...
all-cause mortality in diabetes: the diabetes heart study. Diabetes Care 2011;34:1219–1224