EDITOR’S PAGE

Bridging the Detection Gap Chasm of Risk: Where Can Computed Tomography Angiography Take Us?

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In this issue of *JACC*, a large validation series of the prognostic value of significant coronary artery disease (CAD) by cardiac computed tomographic angiography (CTA) is published (1). This new report adds to our understanding of the prognostic accuracy of CTA measurements of obstructive CAD for risk stratification purposes by including a large consecutive series of 1,667 patients. Placing this data within the context of existing CTA data, we observe improved precision in risk stratification and an obvious separation in events between patients with none-mild CAD compared to those with obstructive CAD. The summary meta-analytic rate for obstructive CAD is more than 10-fold higher than that of patients with none-mild CAD.

When comparing risk stratification with CTA to that of other imaging modalities, interesting patterns illumine a direction for future developments for this modality (Fig. 1)(2–10). The summary meta-analytic rate for obstructive CAD is higher (11.1%, 5.1% to 22.5%) than for that of significant perfusion (6.2%, 5.9% to 6.5%) or inducible wall motion (7.5%, 5% to 13.4%) abnormalities; highlighting the importance of the burden of CAD as the prominent driver for influencing the hazard for cardiovascular events. For CTA, more extensive, severe, and proximal location of obstructive CAD defines higher CAD event rates (11,12). The totality of interaction of obstructive CAD with ischemia as a modulator of risk is unclear. Further the degree to which overlap exists between extensive CAD and severe ischemia is also unclear but remains an important goal for future developments in risk stratification, which will also focus on the interplay between nonischemic CAD to ischemic mild to severe CAD.

CTA has tremendous potential due to its ability to define not only obstructive CAD but to examine the burden of nonobstructive atherosclerosis. By examining the current evidence, the summary CAD event rate for CTA-verified none-mild CAD (1.5%, 0.9% to 2.6%) is decidedly higher when compared to that of no perfusion abnormalities (0.6%). The higher event rate with no obstructive CAD on CTA indicates a threshold of risk for significant stenosis (...or more extensive atherosclerotic disease) that is higher than that for nonobstructive CAD. This threshold needs to be addressed to define the importance/characteristics of nonobstructive atherosclerosis. An example of this is the very low event rate in individuals with a zero coronary artery calcium score (13,14). A gradient of cardiovascular event risk occurs directly proportional to the extent of calcification (13,14). The lack of correlation between obstructive CAD and coronary calcium, yet its important risk stratification ability, identifies the significant risk burden of nonobstructive atherosclerosis. To that end, one can envision even lower event rates for CTA nonobstructive CAD declining from mild coronary lesions, on the high end of this 1.5% event rate, to a very low-risk for those with no plaque, more closely approximating population norms for risk.

Similar to the role of obstructive CAD in defining higher risk status, the characteristics of a nonobstructive plaque should modulate the

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risk spectrum. We have yet to clearly define the graded change in risk with nonobstructive atherosclerosis that occurs below the obstructive CAD threshold. Additionally, within the nonobstructive atherosclerotic disease subsets, features of high-risk plaque may proffer a substantial risk for downstream acute coronary syndromes (ACS). Preliminary evidence suggests that certain plaque characteristics may be definable with CTA and provide an important link to ACS risk including sudden death (15). Novel gains in risk detection may be realized within nonobstructive atherosclerotic disease subsets to define unique subsets whose risk is equivalent to those with obstructive CAD. The defining of CAD risk equivalent status patients, may blur the prominence of symptoms, obstructive disease or perfusion deficit as signifying risk, but identify risk gradation that occurs across the spectrum of nonobstructive and obstructive CAD. Thus, future developments in the field of CTA should focus on improving the granularity of lower and higher risk status including modulation of ischemic risk. A better understanding of the role of CTA in risk detection is fundamental to integrating this modality into every day clinical decision making. Our mandate for the future of cardiac imaging is now to devise strategies to improve the current detection gap that afflicts millions of patients annually in this country and worldwide.

Figure 1. Meta-Analyses of the 1-Year Event Rates

One-year event rates (95% confidence intervals) are presented for no obstructive and obstructive coronary artery disease (CAD) by coronary computed tomography angiography (CTA), and for normal and abnormal stress myocardial perfusion single-photon emission computed tomography (SPECT) and positron emission tomography (PET); data are compiled for SPECT (2), for PET (3,4), and for echocardiography (9,10). The event rates are calculated using a random effects model with significant heterogeneity noted for no obstructive and obstructive CAD (p < 0.0001). Event types are varied by study including death, myocardial infarction, unstable angina, and/or revascularization.

### Study name | N | p value
---|---|---
Pundziute | 100 | 0.01
Min | 1,127 | <0.0001
Gillard | 141 | <0.0001
Gaemperli | 220 | <0.0001
Matsumoto | 810 | <0.0001
Ostrom | 2,538 | <0.0001
Hadamitzky | 1,667 | <0.0001
Summary For CTA | 6,603 | <0.0001

1-Year Event Rates

<table>
<thead>
<tr>
<th>Negative Test Results</th>
<th>Positive Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Obstructive CAD</td>
<td>Obstructive CAD</td>
</tr>
<tr>
<td>0.0%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Normal Perfusion</td>
<td>Abnormal Perfusion</td>
</tr>
<tr>
<td>0.0%</td>
<td>25.0%</td>
</tr>
<tr>
<td>Normal Wall Motion</td>
<td>Abnormal Wall Motion</td>
</tr>
<tr>
<td>0.0%</td>
<td>17.5%</td>
</tr>
<tr>
<td>0.0%</td>
<td>25.0%</td>
</tr>
<tr>
<td>0.0%</td>
<td>4.0%</td>
</tr>
</tbody>
</table>

Summary

For CTA, SPECT / PET, Meta-Analysis

71,463 | <0.0001

Echocardiography, Meta-Analysis

17,078 | <0.0001

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REFERENCES


