

Myocardial Perfusion Imaging has Markedly Lower Sensitivity after Accounting for Verification Bias

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Abstract:

Introduction: Estimates of myocardial perfusion imaging (MPI) performance are often derived from convenience cohorts of patients undergoing coronary angiography, who are selectively referred for this invasive test because of high-risk clinical characteristics, high-risk test results, or both. While clinically appropriate, this approach distorts estimates of MPI's test performance, since sensitivity and specificity are only assessed in patients who are referred for angiography. This verification bias—sometimes called “work-up” or “referral” bias—compromises physicians' ability to appropriately use noninvasive testing since test performance data may be inaccurate. We sought to examine the impact of verification bias on MPI's performance, to provide clinicians with a more accurate assessment of its diagnostic characteristics.

Hypothesis: We hypothesized that the bias-adjusted performance of MPI will show significantly lower sensitivity and significantly higher specificity compared to published estimates derived from convenience cohorts undergoing invasive angiography.

Methods: We used a comprehensive meta-analysis of MPI performance (14 studies totaling 3,500 patients based on angiographic referral) to assess the reported (biased) sensitivity and specificity of MPI. We then computed unbiased sensitivity and specificity rates using published methods, combining the meta-analysis estimates with other published data giving angiography referral rates for patients with both positive and negative MPI results (48% and 6%, respectively). Finally, we validated the unbiased performance estimates using a recent multi-center study (Coronary Obstruction Detection by Molecular Personalized Gene Expression [COMPASS]) of MPI that was not subject to verification bias, since all subjects had angiographic referral to use as the gold standard.

Results: The meta-analysis reported (biased) MPI sensitivity was 81% and specificity was 65%. After appropriate correction for verification bias, the unbiased estimate of sensitivity was 35% (95% CI = 27% to 45%) and specificity was 94% (95% CI = 91% to 96%). These estimates were very similar to the observed values in the unbiased COMPASS trial (N=431 patients): core

laboratory MPI sensitivity was 36% (95% CI = 24% to 50%) and specificity was 90% (95% CI = 87% to 93%).

Conclusions: In conclusion, after correction for verification bias or when estimated in a population without bias, MPI is markedly less sensitive and more specific than most published estimates would indicate. The biased estimates of test performance would tend to encourage referral to angiography compared to corrected estimates. Future studies of non-invasive imaging modalities in patients with suspected or diagnosed CHD should report performance estimates that are either corrected for verification bias or use unbiased cohorts, to provide an accurate assessment of test performance for clinical decision making.

Reference:

Elashoff MR, Ladapo JA, Phelps CE, et al. Myocardial Perfusion Imaging has Markedly Lower Sensitivity after Accounting for Verification Bias. *Circ Cardiovasc Qual Outcomes*. 2013;5:A259.

Abstract Highlights:

- Diagnostic test performance (sensitivity and specificity) is usually not dependent on disease prevalence, but can be subject to referral bias, if only a subset of patients in the population is studied.
- MPI performance values reported in literature are commonly derived from cohorts of patients undergoing coronary angiography who are selectively referred for this invasive test because of high-risk clinical characteristics, abnormal noninvasive test results, or both. However, in real-world clinical practice, patients with negative MPIs are rarely referred for angiography. This observed study bias is known as “verification” or “referral” bias.
- The objective of this study was to examine the impact of verification bias on MPI’s performance in real-world clinical practice, to provide clinicians with a more accurate assessment of its true diagnostic performance.
- Once corrected for verification bias, MPI had markedly lower sensitivity and higher specificity than published estimates suggest: this finding is consistent with the results observed in the recently reported COMPASS trial.*

Should you have any questions related to this study or abstract, please contact CardioDx Medical Affairs at medicalaffairs@cardiodx.com or 866-941-4996.

*Thomas GS, Voros S, McPherson JA, et al. The Compass trial (NCT01117506): A prospective multi-center, double-blind study assessing a whole blood gene expression test for the detection of obstructive coronary artery disease in symptomatic patients referred for myocardial perfusion imaging. *Circulation*. 2011;124:A11106.