Changing epidemiology of CAD: Why should we pay attention?

Marcelo F. Di Carli, MD^{a,b,c,d}

^a Cardiovascular Imaging Program, Departments of Radiology and Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston

^b Division of Nuclear Medicine and Cardiovascular Imaging, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston

^c Division of Cardiovascular Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston

^d Brigham and Women's Hospital, Boston, MA

Received Jan 21, 2021; accepted Jan 22, 2021
doi:10.1007/s12350-021-02560-7

Radionuclide myocardial perfusion imaging (MPI) has proven to be an indispensable tool that transformed management of patients with suspected or known coronary artery disease (CAD) for more than 40 years. However, there are powerful signs that the epidemiology and clinical manifestations of CAD are changing and that the paradigm that served as the bedrock principle for the effectiveness of radionuclide MPI for many decades—that is the search for obstructive CAD—may be insufficient to adequately evaluate patients with stable chest pain syndrome in modern cardiovascular medicine.

First, there is emerging evidence that the frequency of obstructive CAD as a key driver of symptoms and clinical outcomes is declining. Indeed, over the last two decades, diagnostic yields for invasive coronary angiography,^{1,2} and noninvasive stress testing have fallen.^{3,4} In one large registry of patients with angina referred for coronary angiography, the rate of nonobstructive atherosclerosis as the principal underlying angiographic phenotype increased by 20% to 40% over a 10-year period in both women and men.¹ Recent data from Olmstead County, MN have also documented a steady decline in angiographically obstructive CAD over the last two decades.⁵ This is consistent with other data from large registries⁶ and a recent clinical trial.⁷

Second, the growing controversy about the clinical utility of probability scores as an aid to diagnosis of

obstructive CAD in stable symptomatic patients—once standard practice in cardiology—seems consistent with the declining prevalence of obstructive CAD. Indeed, multiple recent studies in the contemporary era have concluded that many of these scores lead to a significant overestimation of the pre-test likelihood of obstructive CAD.^{8–11} In fact, the recent iteration of the National Institute for Health and Care Excellence (NICE) guideline in the United Kingdom suggests that Bayesian probability analysis should not be used to guide decisions regarding noninvasive testing for patients with stable chest pain.¹²

Third, the incidence of acute presentations of atherothrombotic plaque rupture causing myocardial infarction (MI), particularly with ST-segment elevation, has decreased,¹³ while the rates of hospitalizations with a secondary MI diagnosis¹⁴ and heart failure with preserved ejection fraction¹⁵ have risen sharply. These secondary causes of MI have been associated with heart failure, atrial fibrillation, diabetes and chronic kidney disease and affect a large segment of the population. Although secondary causes of MI have traditionally been associated with older age, similar findings have been reported in patients suffering an MI before 50 years of age.¹⁶ Meanwhile these observations are occurring in a context of important changes in patient demographics, epidemiologic shifts in the prevalence of cardiometabolic risk factors in the population including the epidemic of obesity, diabetes and related metabolic disorders.¹⁷ The epidemic of cardiometabolic disease has been associated with an anatomic phenotype dominated by 'diffuse atherosclerosis' and 'microvascular remodeling'.¹⁸

Reprint requests: Marcelo F. Di Carli, MD, Brigham and Women's Hospital, 75 Francis St, ASB-L1 Room 037-C, Boston, MA 02115; mdicarli@bwh.harvard.edu

J Nucl Cardiol 2021;28:386–8.

1071-3581/\$34.00

Copyright © 2021 American Society of Nuclear Cardiology.

Fourth, the observed temporal decline in the rate of abnormal SPECT MPI studies⁴ with a marked reduction in the proportion of high-risk scans and a proportional increase in apparently ‘low-risk’ tests³ appear to be in line with all secular changes described above. It is not surprising that an anatomic phenotype characterized by diffuse nonobstructive atherosclerosis and microvascular disease would be relatively invisible for our traditional radionuclide semi-quantitative MPI approach designed to uncover focal obstructive CAD. While the observations described above may be perceived as ‘good news’, the emerging evidence suggest that the rise in diffuse atherosclerosis and microvascular disease are also associated with significant adverse outcomes.¹⁷

Consequently, it is imperative that we pay attention to and acknowledge the changes described above and, more importantly, reflect on their implications for patient care. The shifting paradigm away from the dominant role of obstructive CAD presents formidable challenges for our traditional approach to CAD evaluation with radionuclide MPI. So, we must dig deeper in our toolbox to find solutions. The pioneering work of Schelbert and Gould in the early 1980s introducing the possibility of quantitative myocardial blood flow imaging noninvasively with radionuclide imaging provided the field of nuclear cardiology with a powerful tool that now—nearly 40 years later—will prove to be indispensable in the evaluation of ischemic heart disease. Quantification of myocardial blood flow offers a powerful opportunity to tackle these challenges effectively and we need to quickly embrace such changes to maintain the transformative role of nuclear cardiology in patient care and research.

Disclosures

Dr. Di Carli receives investigator-initiated grant support from Gilead Sciences and Spectrum Dynamics, and consulting fees from Bayer and Janssen.

References

- Jespersen L, Hvelplund A, Abildstrom SZ, Pedersen F, Galatius S, Madsen JK, Jorgensen E, Kelbaek H, Prescott E. Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events. *Eur Heart J* 2012;33:734-44.
- Maddox TM, Stanislawski MA, Grunwald GK, Bradley SM, Ho PM, Tsai TT, Patel MR, Sandhu A, Valle J, Magid DJ, Leon B, Bhatt DL, Fihn SD, Rumsfeld JS. Nonobstructive coronary artery disease and risk of myocardial infarction. *JAMA* 2014;312:1754-63.
- Jouni H, Askew JW, Crusan DJ, Miller TD, Gibbons RJ. Temporal trends of single-photon emission computed tomography myocardial perfusion imaging in patients with coronary artery disease: A 22-year experience from a tertiary academic medical center. *Circ Cardiovasc Imaging* 2017. <https://doi.org/10.1161/circimaging.116.005628>.
- Rozanski A, Gransar H, Hayes SW, Min J, Friedman JD, Thomson LE, Berman DS. Temporal trends in the frequency of inducible myocardial ischemia during cardiac stress testing: 1991 to 2009. *J Am Coll Cardiol* 2013;61:1054-65.
- Gerber Y, Gibbons RJ, Weston SA, Fabbri M, Herrmann J, Manemann SM, Frye RL, Asleh R, Greason K, Killian JM, Roger VL. Coronary disease surveillance in the community: Angiography and revascularization. *J Am Heart Assoc* 2020;9:e015231.
- Patel MR, Dai D, Hernandez AF, Douglas PS, Messenger J, Garratt KN, Maddox TM, Peterson ED, Roe MT. Prevalence and predictors of nonobstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. *Am Heart J* 2014;167:e2.
- Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, Cole J, Dolor RJ, Fordyce CB, Huang M, Khan MA, Kosinski AS, Krucoff MW, Malhotra V, Picard MH, Udelson JE, Velazquez EJ, Yow E, Cooper LS, Lee KL, PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 2015;372:1291-300.
- Bittencourt MS, Hultén E, Polonsky TS, Hoffman U, Nasir K, Abbasa S, Di Carli M, Blankstein R. European Society of Cardiology-Recommended Coronary Artery Disease Consortium pretest probability scores more accurately predict obstructive coronary disease and cardiovascular events than the Diamond and Forrester Score: The Partners Registry. *Circulation* 2016;134:201-11.
- Cheng VY, Berman DS, Rozanski A, Dunning AM, Achenbach S, Al-Mallah M, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, Chinnaiyan K, Chow BJ, Delago A, Gomez M, Hadamitzky M, Hausleiter J, Karlsberg RP, Kaufmann P, Lin FY, Maffei E, Raff GL, Villines TC, Shaw LJ, Min JK. Performance of the traditional age, sex, and angina typicality-based approach for estimating pretest probability of angiographically significant coronary artery disease in patients undergoing coronary computed tomographic angiography: Results from the multinational coronary CT angiography evaluation for clinical outcomes: An international multicenter registry (CONFIRM). *Circulation* 2011;124:1-8.
- Genders TS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, Galema TW, Meijboom WB, Mollet NR, de Feyter PJ, Cademartiri F, Maffei E, Dewey M, Zimmermann E, Laule M, Pugliese F, Barbagallo R, Sinitsyn V, Bogaert J, Goetschalckx K, Schoepf UJ, Rowe GW, Schuijff JD, Bax JJ, de Graaf FR, Knuuti J, Kajander S, van Mieghem CA, Meijs MF, Cramer MJ, Gopalan D, Feuchtnner G, Friedrich G, Krestin GP, Hunink MG, CAD Consortium. A clinical prediction rule for the diagnosis of coronary artery disease: Validation, updating, and extension. *Eur Heart J* 2011;32:1316-30.
- Genders TS, Steyerberg EW, Hunink MG, Nieman K, Galema TW, Mollet NR, de Feyter PJ, Krestin GP, Alkadhi H, Leschka S, Desbiolles L, Meijs MF, Cramer MJ, Knuuti J, Kajander S, Bogaert J, Goetschalckx K, Cademartiri F, Maffei E, Martini C, Seitun S, Aldrovandi A, Wildermuth S, Stinn B, Fornaro J, Feuchtnner G, De Zordo T, Auer T, Plank F, Friedrich G, Pugliese F, Petersen SE, Davies LC, Schoepf UJ, Rowe GW, van Mieghem CA, van Driessche L, Sinitsyn V, Gopalan D, Nikolaou K, Bamberg F, Cury RC, Battle J, Maurovich-Horvat P, Bartykowszki A, Merkely B, Becker D, Hadamitzky M, Hausleiter J, Dewey M, Zimmermann E, Laule M. Prediction model to estimate presence of coronary artery disease: Retrospective pooled analysis of existing cohorts. *BMJ* 2012;344:e3485.
- National Institute of Health and Clinical Excellence. Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain

- or discomfort of suspected cardiac origin (update). Clinical guideline 95. London: NICE; 2016.
13. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med* 2010;362:2155-65.
 14. Sacks NC, Ash AS, Ghosh K, Rosen AK, Wong JB, Rosen AB. Trends in acute myocardial infarction hospitalizations: Are we seeing the whole picture? *Am Heart J* 2015;170:1211-9.
 15. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 2006;355:251-9.
 16. Singh A, Gupta A, DeFilippis EM, Qamar A, Biery DW, Almarzooq Z, Collins B, Fatima A, Jackson C, Galazka P, Ramsis M, Pipilas DC, Divakaran S, Cawley M, Hainer J, Klein J, Jarolim P, Nasir K, Januzzi JL, Di Carli MF, Bhatt DL, Blankstein R. Cardiovascular mortality after type 1 and type 2 myocardial infarction in young adults. *J Am Coll Cardiol* 2020;75:1003-13.
 17. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Shay CM, Spartano NL, Stokes A, Tirschwell DL, VanWagner LB, Tsao CW, American Heart Association Council on Epidemiology, Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2020 update: A Report from the American Heart Association. *Circulation* 2020;141:e139-596.
 18. Roberts WC. Quantitative extent of atherosclerotic plaque in the major epicardial coronary arteries in patients with fatal coronary heart disease, in coronary endarterectomy specimens, in aorta-coronary saphenous venous conduits, and means to prevent the plaques: A review after studying the coronary arteries for 50 years. *Am J Cardiol* 2018;121:1413-35.
- Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.