

Avoiding Unnecessary Coronary Angiographic Studies but Getting the Balance Right

Evitar estudios invasivos innecesarios en pacientes con angina estable pero sin perder de vista el objetivo principal

JUAN CARLOS KASKJ¹, FRCP, FESC, FACC, FAHA

The occurrence of typical angina pectoris in individuals without obstructive coronary artery disease is common, as attested by results of large studies. (1)

Although most guidelines for triaging patients for cardiac catheterization recommend risk assessment and noninvasive testing, some guidelines recommend proceeding directly to coronary arteriography in specific patient subgroups. The aim of avoiding unnecessary invasive investigations is laudable, as it should reduce both risk and costs associated with the procedure. Of interest, Patel et al (1) carried out a study in 398,978 patients (median age 61 years; 53% men) without known coronary artery disease (CAD) who were undergoing elective catheterization. The patients' clinical characteristics, conventional risk factors (26.0% had diabetes, and 70% had hypertension), angina symptoms and the results of noninvasive diagnostic testing were correlated with the presence of obstructive CAD (>70% diameter reduction). Noninvasive testing was performed in 84% of the patients. Of importance, angiography showed that only 37.6% of patients had obstructive CAD and almost 40% of patients had no CAD (defined as < 20% stenosis in all vessels). As expected, independent predictors of obstructive CAD were male sex, older age, insulin-dependent diabetes and dyslipidemia. Very interestingly, patients with a positive result on a noninvasive test –indicative of myocardial ischemia– were only moderately more likely to have CAD than those who did not undergo any testing. Thus in the Patel study (1) only a little more than one third of patients without known disease who underwent elective cardiac catheterization had obstructive CAD, but most of them had angina and a positive result of non-invasive testing for ischemia.

In this issue of the Journal, Kevorkian et al. (2) analyzed consecutive diagnostic coronary angiographies for suspected CAD in 12,686 admitted patients in five

centers of Buenos Aires and report data of 3,990 included patients with suspected stable coronary disease.

They aimed at identifying ways of minimizing unnecessary invasive procedures thus limiting “associated risk and increased health costs”. Albeit a retrospective study, the results are quite similar to those in the Patel study (1) regarding the yield of coronary arteriography, as 38.6% of patients had a normal angiogram. Female gender, younger age and absence of ischemic symptoms were associated with a higher likelihood of a normal coronary angiogram. Kevorkian et al. conclude that in stable angina patients referred for diagnostic angiography, female gender, younger age and the absence of symptoms, were associated with angiographically “normal” coronary arteries and argue the case for a better use of clinical stratification models to detect patients with significant CAD, thus limiting unnecessary invasive studies. These findings are important and highlight the crucial role of proper clinical characterization of angina patients, even in this time and age when technological advances may give the impression that clinical assessment of patients is a thing of the past. Despite the great importance of these findings, however, and the laudable objectives of both Patel et al (1) and Kevorkian et al (2) they –in my view– have omitted discussing an important point in their evaluation of the results, and this is that ruling out obstructive CAD –albeit great news for both physicians and patients– is not the full answer to the patients' problem. In the absence of CAD, ischemia can still be present and coronary arteriography can be necessary to rule out dynamic causes of chest pain and myocardial ischemia, such as microvascular angina (3).

MICROVASCULAR ANGINA

Contrary to the epicardial coronary vasculature, the coronary microcirculation has remained elusive to con-

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Director, Cardiovascular and Cell Sciences Research Institute, St George's, University of London, London, United Kingdom

FRCP Fellow of the Royal College of Physicians

FESC Fellow of the European Society of Cardiology

FACC Fellow of the American College of Cardiology

FAHA Fellow of the American Heart Association

ventional imaging techniques, as we have argued in a recent review article (4) and cardiologists have not given coronary microvascular dysfunction (CMVD) as much attention as epicardial CAD has received so far. Indeed, the condition often referred to as 'chest pain with normal coronary arteries' or 'cardiac syndrome X' (CSX) (5,6) has puzzled physicians over the years. CMVD is often present in patients with chronic stable angina and/or dyspnea with and without CAD (7,8). The term 'microvascular angina' (3) was coined in an effort to define the underlying functional abnormality in patients with chest pain and normal coronary arteries. Documenting abnormal coronary microvascular responses to functional testing with the reproduction of symptoms is critical for the diagnosis. Of note, as shown by the ACOVA study (9), intracoronary acetylcholine (ACH) elicits diffuse epicardial vasoconstriction ($\geq 75\%$ diameter reduction) and/or microvascular spasm with the reproduction of the patient's symptoms as well as ECG changes in a large proportion of patients with chest pain despite angiographically normal coronary arteries. Findings in the ACOVA study (9) are of importance as they point towards a continuum of abnormal coronary vasomotion playing a role in the pathogenesis of angina in CSX. Previous studies have shown that a reduced vasodilatory capacity of the coronary microcirculation can lead to exercise-induced angina in CSX (3-8) and recent observations indicate that some CSX patients may share features of Prinzmetal's variant angina (9). Distal diffuse epicardial spasm as well as microvascular spasm are the mechanisms underlying symptoms in a large proportion of patients with stable angina and/or angina at rest who have no obstructive CAD. Administration of ACH during coronary arteriography can identify the reason for the anginal symptoms in these patients and lead to a more rational management. Indeed, the infusion of ACH in our studies resulted in both ischemic ST-segment changes, mainly ST-segment depression, and the reproduction of the usual chest discomfort experienced by the patients during daily life. (9) In my view, the ACH-test should be carried out routinely for the assessment of patients with chest pain despite angiographically normal coronary arteries as it may be useful to identify increased coronary constriction as the mechanism for their angina and the administration of appropriate therapy, e.g. calcium channel blockers, nicorandil, ranolazine, PDE-inhibitors, endothelin receptor antagonists and fasudil, which may reduce the frequency and severity of the anginal episodes. Interventional cardiologists should train as appropriate to carry out these tests safely.

In summary, clinical characterization of anginal symptoms and risk stratification is of importance to avoid unnecessary invasive procedures. However, coronary arteriography may be useful not only to rule

out obstructive CAD but also to identify functional epicardial and coronary microvascular abnormalities in a diversity of clinical settings. Functional coronary microvascular abnormalities such as abnormal vasodilation and coronary spasm often explain the signs and symptoms of myocardial ischemia in individuals with normal coronary angiograms. Therefore, an assessment of CMVD should be considered to be of paramount importance in the evaluation of angina patients, particularly those with normal coronary arteries or non-obstructive CAD. The finding of non-obstructive CAD at angiography should not be the end of the diagnostic road, and functional mechanisms, often responsible for angina, need to be investigated further. If coronary arteriography is considered to be indicated after a careful clinical characterisation of the patient, as suggested by Kevorkian et al (2) in this issue of the Journal, interventionists should be also prepared to carry out functional studies, including tests of vasoconstriction (i.e. ACH) to rule out causes of myocardial ischemia often missed because functional studies are not carried out during angiography. In patients with angina pectoris, the finding of angiographically normal coronary arteries should represent the starting point for functional coronary investigations.

Conflicts of interest

None declared

REFERENCES

1. Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, et al. Low diagnostic yield of elective coronary angiography. *N Engl J Med* 2010;362:886-95. <http://doi.org/d8ccd7>
2. Kevorkian R, Carlevaro O, Puerta L, Dionisio G, Etcheverry C, Blanco P, et al. Predictors of Angiographically Normal Coronary Arteries in Stable Patients with Suspected Coronary Disease. *Rev Argent Cardiol* 2015;83:25-30.
3. Cannon RO III, Epstein SE. 'Microvascular angina' as a cause of chest pain with angiographically normal coronary arteries. *Am J Cardiol* 1988;61:1338-43. <http://doi.org/d98bgg>
4. Herrmann J, Kaski JC, Lerman A. Coronary microvascular dysfunction in the clinical setting: From mystery to reality. *Eur Heart J* 2012; 33:2771-82. <http://doi.org/kvp>
5. Kaski JC. Pathophysiology and management of patients with chest pain and normal coronary arteriograms (cardiac syndrome X). *Circulation* 2004;109:568-72. <http://doi.org/bcm9qh>
6. Kaski JC, Aldama G, Cosin-Sales J. Cardiac syndrome X. Diagnosis, pathogenesis and management. *Am J Cardiovasc Drugs* 2004;4:179-94. <http://doi.org/c6ftfc>
7. Camici PG, Crea F. Coronary microvascular dysfunction. *N Engl J Med* 2007;356:830-40. <http://doi.org/bm7gfg>
8. Lanza GA, Crea F. Primary coronary microvascular dysfunction: clinical presentation, pathophysiology, and management. *Circulation* 2010;121:2317-25. <http://doi.org/fwd4jd>
9. Ong P, Athanasiadis A, Borgulya G, Mahrholdt H, Kaski JC, Sechtem U. High prevalence of a pathological response to acetylcholine testing in patients with stable angina pectoris and unobstructed coronary arteries. The ACOVA Study (Abnormal COronaryVASomotion in patients with stable angina and coronary arteries). *J Am Coll Cardiol* 2012;59:655-62. <http://doi.org/m9h>