

A new algorithm for the management of stable coronary artery disease incorporating CT coronary angiography and fractional flow reserve: how we can improve outcomes and reduce costs

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Coronary atherosclerosis is a major cause of morbidity and mortality. On diagnosis, all patients require appropriate lifestyle modification and lifelong drug therapy with aspirin, statins, and angiotensin-converting enzyme inhibitors plus β -blockers if their heart has been damaged. Instituting these measures is estimated to reduce adverse cardiovascular events by 75%–80% over a 5-year period.¹ Revascularisation by percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery plays an important role, but it is a double-edged sword. In the presence of significant myocardial ischaemia, revascularisation reduces symptoms^{2,3} and improves prognosis,^{4,6} but in its absence revascularisation worsens outcomes, even when the coronary lesion in question may have a diameter stenosis of 70% or greater.^{7,8}

In Australia, as in other countries,⁹ most coronary lesions are revascularised on the basis of their angiographic characteristics, often without knowledge of whether the lesion is causing ischaemia or not. As such, many coronary lesions that are not physiologically significant are unnecessarily stented or bypassed, at considerable expense to the health system and to the detriment of the patient. Fortunately, new technology, namely computed tomography coronary angiography (CTCA) and measurement of coronary fractional flow reserve (FFR), if correctly applied, enables more accurate assessment of coronary anatomy and function and has the potential to substantially improve outcomes and lower costs. Here, we present and discuss a simple algorithm (Box 1) for the management of stable coronary artery disease (CAD) using this new technology.

Diagnosis of coronary atherosclerosis

The presence of coronary atherosclerosis can be assumed if the patient has presented with a proven acute coronary syndrome or has evidence of atherosclerosis elsewhere. In other circumstances, such as symptomatic patients or patients with multiple risk factors in whom CAD is suspected but not proven, diagnosis is less straightforward. The most reliable diagnostic test is a 64-slice (or higher) CTCA scan, which excludes significant CAD with a sensitivity and negative predictive value in excess of 96%.¹⁰ Atherosclerosis is predominantly a disease of the arterial wall, which may encroach on the vessel lumen over time. CTCA provides accurate information about the state of both the arterial wall and the lumen. A normal CTCA scan effectively excludes coronary atherosclerosis and portends an extremely low likelihood of coronary events over at least the next 5 years.¹¹ If the CTCA scan shows atherosclerosis, but no luminal stenosis of greater than 50%, medical treatment (as described above) should be initiated. If the CTCA scan shows lesions of 50% or greater severity, then further testing for ischaemia may be appropriate (Box 1).

Coronary atherosclerosis cannot be cured and requires lifelong medical therapy. Once a diagnosis has been made, the only continuing diagnostic issue is that of myocardial ischaemia, for

ABSTRACT

- Computed tomography coronary angiography is the most reliable diagnostic test for coronary atherosclerosis. Stress testing should be reserved for diagnosis of myocardial ischaemia.
- Revascularisation, either by stenting or bypass grafts, is commonly performed in patients with stable coronary artery disease but is a double-edged sword. In the presence of ischaemia, revascularisation improves outcomes; in its absence, outcomes are worsened.
- In current practice, the decision of whether to revascularise is mainly made on the basis of the angiographic appearance of the coronary lesion in question. Physiological assessment of coronary lesions by the use of a pressure wire and measurement of fractional flow reserve (FFR) often shows that lesions thought to be sufficiently severe to warrant stenting or bypass do not cause ischaemia.
- A recent randomised study has shown that using FFR measurements to guide coronary stenting resulted in a lower use of stents, decreased costs and superior outcomes at 2 years, compared with traditional angiographic assessment alone.
- We believe that changes to the methods of health reimbursement are needed in both the public and private health systems, to facilitate greater use of FFR measurement.

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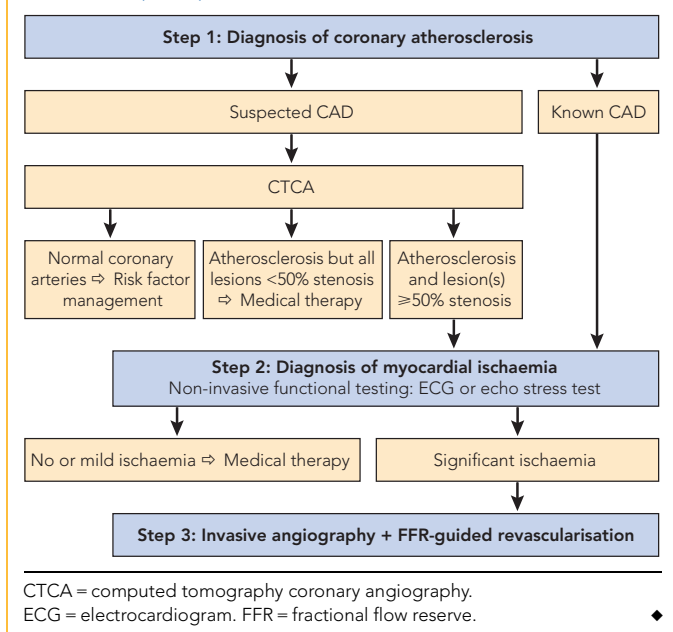


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which CTCA is not the appropriate test.¹² Therefore, subsequent CTCA scans, which are expensive (\$500) and carry a radiation burden (although less than that of nuclear stress testing and invasive angiography¹³), are not indicated.

Although commonly used for this purpose, neither stress testing nor invasive coronary angiography are appropriate tests for diagnosing coronary atherosclerosis. A negative stress test does not exclude coronary atherosclerosis requiring medical therapy. Invasive coronary angiography gives precise information about the coronary arterial lumen but does not examine the arterial wall. As such, a “normal” invasive coronary angiogram does not exclude coronary atherosclerosis. Invasive coronary angiography should only be performed if there is an intention of performing revascularisation, and therefore its use should be restricted to interventional cardiologists. The common practice of non-interventional cardiologists performing “diagnostic” coronary angiography (cost, \$865) and then referring the patient to an interventional cardiologist if obstructive lesions are found is wasteful and exposes patients to unnecessary radiation and risk.

1 Algorithm for management of stable coronary artery disease (CAD)



Diagnosis of myocardial ischaemia

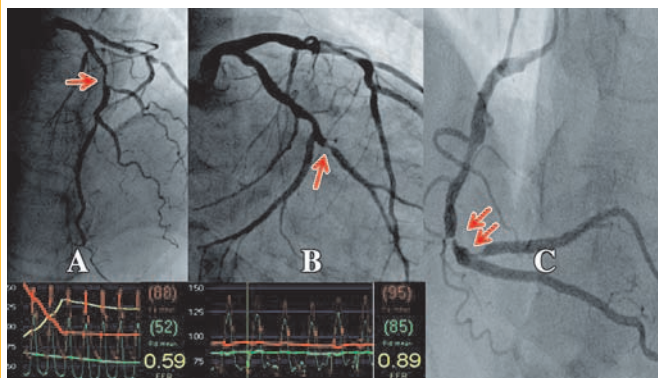
The presence of myocardial ischaemia can be assumed if a patient with known CAD has typical angina. In other cases, stress testing is the standard non-invasive means of diagnosing ischaemia. Irrespective of the type of stress test (standard electrocardiogram [ECG], nuclear stress test or echo stress test) used, a negative test result at a satisfactory workload effectively excludes any myocardial ischaemia significant enough to warrant intervention, and obviates the need for invasive angiography. Depending on the clinical circumstances, a positive test result is an indication for further investigation with invasive angiography (Box 1).

In most circumstances, the less expensive ECG exercise test (cost, \$144) is adequate screening for this purpose,¹⁴ but in patients with a resting ECG abnormality or those unable to exercise, nuclear (cost, \$984) or echo (cost, \$406) stress tests are a more accurate means of assessing ischaemia. Both these tests have the additional advantage of localising the area of ischaemia; however, this attribute is now of limited value because FFR^{7,15} offers a more precise means of achieving this, particularly in multivessel CAD.¹⁶⁻¹⁸ Nuclear and echo stress tests provide comparable information with respect to myocardial ischaemia, but nuclear stress tests are more expensive and carry a significant radiation burden,¹³ and should therefore no longer be used for this purpose.

Assessment of myocardial ischaemia using FFR

An important recent advance has been the ability to accurately determine the physiological significance of an individual coronary lesion by measuring FFR.^{7,15} FFR is defined as the ratio between coronary pressure distal to the stenosis in question and aortic pressure measured simultaneously during adenosine-induced hyperaemia. Coronary pressure is obtained by passing a pressure guide wire distal to the coronary stenosis in a manner analogous to passing a guide wire for the purpose of PCI.^{7,15} As such, it can be

2 Example of coronary fractional flow reserve (FFR) assessment in multivessel disease



A 60-year-old man with a background of hypertension, hyperlipidaemia and stable angina underwent invasive coronary angiography and FFR assessment before percutaneous coronary intervention (PCI). Angiography of each major epicardial vessel and the corresponding FFR are shown. The pressure tracing shows the aortic pressure (red) and distal coronary pressure (green), allowing calculation of the FFR (yellow number).

A: Stenosis in the mid left anterior descending (LAD) artery with 70% diameter stenosis (arrow) upon visual assessment. The aortic and distal coronary pressures are widely split, with an FFR of 0.59.

B: Stenosis in the ongoing marginal branch of the left circumflex (LCx) artery. Diameter stenosis is 70% (arrow), with an FFR of 0.89.

C: Serial stenoses in the mid right coronary artery (RCA) and ostium of the posterolateral branch (arrows). Both lesions were judged to be > 90% and were stented (with one long stent) without an FFR measurement.

Based on angiographic criteria alone, revascularisation would be indicated in the four lesions in the three arteries. Using an evidence-based approach with FFR guidance, PCI was performed in arteries with an FFR ≤ 0.80, namely the LAD artery and RCA, but not the LCx artery. ♦

easily and safely performed by those experienced in performing PCI. If PCI is indicated as a result of the FFR measurement, the coronary pressure wire can be used for stent delivery. In the case of multiple lesions in one or more vessels, each individual lesion can be examined by the pressure wire (Box 2). In this way, the lesion or lesions causing ischaemia can be determined in a more precise manner than the traditional method of correlating the angiographic findings with the results of stress testing, or by using angiographic criteria alone.

A wealth of data has validated the accuracy of FFR as a measure of myocardial ischaemia.^{7,15,19} An FFR value of ≤ 0.80 identifies ischaemia-causing coronary stenoses with an accuracy of greater than 90%. An FFR > 0.80 excludes ischaemia with a predictive accuracy of 95%.¹⁵

Clinical utility of FFR

Several important studies have conclusively demonstrated the clinical utility of FFR in decision making concerning PCI.^{7,20} The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study demonstrated that FFR guidance of coronary artery stenting in patients with multivessel disease resulted in a significantly lower rate of adverse events than traditional angiography-guided PCI. In the FAME study, 1005 patients with multives-

sel CAD were randomly assigned to undergo PCI guided by angiography alone or with the addition of FFR measurements.⁷ Before randomisation, lesions thought to require PCI were identified based on their angiographic appearance. Patients randomly assigned to the angiography-guided PCI group underwent stenting of all indicated lesions, whereas those randomly assigned to FFR-guided PCI underwent stenting of indicated lesions only if the FFR was ≤ 0.80 . The results are shown in Box 3 and demonstrate that, in this representative group of patients, the use of FFR resulted in significantly improved outcomes at significantly lower costs.²¹

An important observation in the FAME study was that 65% of lesions judged on angiographic criteria to be between 50% and 70% in severity, and 20% of lesions between 71% and 90% in severity were not physiologically significant based on FFR criteria.²² These angiographically but not physiologically significant lesions accounted for 36% of stented lesions in the angiographic arm of the FAME study.²² Extrapolation of these data leads to the conclusion that more than a third of elective stenting in stable multivessel CAD is unnecessary, potentially harmful and costly to the health system.

Invasive angiography plus FFR-guided revascularisation

In light of the results of the FAME study, patients with stable CAD should undergo coronary angiography with a view to FFR-guided revascularisation if they are found to have significant myocardial ischaemia (Box 1). Angiographic lesions of $>90\%$ severity can be assumed to be ischaemia-generating and can be appropriately revascularised without resort to FFR.²² Likewise, a single lesion in a single vessel with ischaemia demonstrated by stress testing can be appropriately stented without measurement of FFR. It is likely that these two circumstances account for less than 25% of cases. All other coronary lesions should be stented or bypassed only if the FFR is ≤ 0.80 .

What is the current role of FFR in Australia?

Coronary pressure wires to measure FFR have been available in Australia for over 5 years but, according to Medicare statistics, are used in $<5\%$ of cases.²³ There are several reasons for this low uptake. The cost of a pressure wire is \$1300, compared with \$300 for a standard wire. In the public system, where there is no separate diagnosis-related group for procedures involving the pressure wire, casemix funding discourages the use of more expensive equipment, even when the use of that equipment may save money in the long term. In the private system, health insurance companies either do not or only partially cover the cost of the pressure wire. Thus, although the use of a pressure wire saves substantial amounts of money, the method of reimbursement in both the public and private systems militates against its use.

A further disincentive to the use of the pressure wire in the private system is that the Medicare item number for coronary angiography with use of a pressure wire pays less than the item number for PCI and stent(s). Faced with a 50%–70% coronary stenosis, it is easier and more remunerative for an interventional cardiologist to stent the lesion rather than measure FFR, particularly when there is around a 66% chance that the FFR result would show no need for the stent.

What changes are needed to reduce costs and improve outcomes?

Implementation of the management strategy outlined in Box 1 would result in more CTCA scans, but the additional expense related to this would be minor in comparison to the savings that would be achieved if the measures listed in Box 4 were to be adopted. Furthermore, by eliminating nuclear stress tests, “diagnostic” coronary angiography and unnecessary stenting, patient outcomes would be improved and radiation burden reduced. The pros and cons of this approach are summarised in Box 5.

3 FAME study results²¹

Procedural results	Angiography group (n = 496)	FFR group (n = 509)	P
	Mean \pm SD	Mean \pm SD	
Procedure time (min)	70 \pm 44	71 \pm 43	0.51
Contrast agent used (mL)	301 \pm 127	272 \pm 133	<0.001
Stents used per patient	2.7 \pm 1.2	1.9 \pm 1.3	<0.001
Mean procedure and incremental health care costs at 1 year (US\$)	\$14 357	\$12 291	<0.001
Outcomes at 2 years	No. (%)	No. (%)	P
Death	19 (3.8%)	13 (2.6%)	0.25
Myocardial infarction	49 (9.9%)	31 (6.1%)	0.03
Death or myocardial infarction	64 (12.9%)	43 (8.4%)	0.02
Freedom from angina*	332 (75.8%)	369 (79.9%)	0.14

FAME = Fractional Flow Reserve Versus Angiography for Multivessel Evaluation. FFR = fractional flow reserve. * Patients with missing information on angina status were excluded from the analysis. \blacklozenge

4 Measures that would reduce costs

- Confining stress tests to the diagnosis of myocardial ischaemia in known coronary artery disease (CAD)
- Greater reliance on the standard electrocardiogram stress test
- Replacement of nuclear stress tests with stress echocardiography
- Elimination of “diagnostic” invasive coronary angiography
- Routine use of fractional flow reserve measurement in multilesion CAD to avoid unnecessary stenting \blacklozenge

5 Pros and cons of the proposed management strategy

Pros

- More accurate identification of coronary artery disease
- Improved patient outcomes
- Reduced overall costs
- Lower radiation burden

Cons

- Greater reliance on computed tomography coronary angiography — image quality may be variable \blacklozenge

6 Suggested changes to the health system

- The Medicare item number for nuclear stress tests should be abolished
- There should be a Medicare item number for computed tomography coronary angiography, but this should only be applicable to an individual with no known coronary artery disease and only once every 5 years
- Use of the Medicare item number for coronary angiography should be confined to accredited interventional cardiologists
- There should be separate diagnosis-related groups and Medicare item numbers for coronary angiography with the use of a pressure wire and percutaneous coronary intervention (PCI) with the use of a pressure wire
- Hospitals and cardiologists performing PCIs should be accredited to do so, with continuing accreditation based on robust quality assurance programs ◆

Changes to the health system that would facilitate a more evidence-based and cost-effective approach to the management of stable CAD are listed in Box 6. These changes are likely to be opposed by nuclear physicians and sections of the cardiology community. Nevertheless, in our opinion, instituting these changes would undoubtedly result in improved outcomes and substantial savings.

Competing interests

None identified.

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