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REVIEW ARTICLE

Radical changes to the investigation of stable chest pain following the 2016 NICE update

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ABSTRACT

The 2016 National Institute for Health and Care Excellence (NICE) guidelines mark a radical change in the diagnosis of patients with stable chest pain. Quantitative assessments of the disease probability are no longer considered necessary to determine the need and type of diagnostic testing. Instead, the recommendation is for no diagnostic test if the chest pain is judged to be “non-anginal” and CT coronary angiography (CTCA) in patients with “typical” or “atypical” chest pain. The new emphasis on anatomical, rather than functional testing is driven by the accuracy, safety and cost effectiveness of the different investigations as evaluated by NICE. Despite inevitable resource implications NICE calculates that annual savings will be significant.

INTRODUCTION

Since the introduction of selective coronary angiography by Mason Sones in the early 1960s invasive coronary angiography (ICA) has become the reference investigation for chest pain by which all other investigations have been compared.¹ However, despite its advantages of high spatial and temporal resolution it is not without its limitations. By its very nature it is a two-dimensional “lumenogram” which only shows atheroma that impinges on the inner vessel wall. As atheroma brings about a process of positive remodelling significant atheromatous burden can be present before a significant luminal narrowing occurs. This important disease is invisible to invasive angiography. In addition, ICA is an expensive, invasive procedure carrying a recognised morbidity and mortality and strategies are therefore typically utilised to limit the number of patients without obstructive coronary artery disease (CAD) who undergo ICA. With the multitude of non-invasive tests available, ICA is only rarely required to confirm the diagnosis of obstructive CAD and should be reserved for those who are likely to undergo coronary intervention.

In patients with suspected angina, international guidelines have^{2–4} recommended a careful history to determine symptoms and an estimation of disease probability, based on typicality of symptoms, risk factors and the age and sex of the patient, to guide the need for diagnostic testing.⁵ Non-invasive tests can be categorised as “anatomical”

[Cardiac Computed Tomographic Angiography (CCTA)], while the other tests provide “functional” information about stress-induced perfusion defects, wall motion abnormalities or electrocardiogram (ECG) changes as evidence of ischaemia caused by obstructive coronary disease.

The debate as to which non-invasive test is best has raged for decades with divergent opinion. Such debates evolve as new technologies such as CTCA and CTCA fractional flow reserve (FFR_{CT}) appear. When considering the evidence for the diagnostic tests one should remember that for sensitivity and specificity data for a diagnostic test one has to compare a gold standard. Inevitably, for comparison of diagnostic tests for chest pain, ICA is the accepted standard despite its known limitations. Also the performance of any investigation will depend on the population studied. Whilst the sensitivity and specificity of any one test can be considered fixed, the positive and negative predictive value (how likely is a patient with a positive or negative result is likely to have or not have the disease) will vary considerably dependent on the prevalence of disease in the population studied. As such studies of subgroups of populations give little indication of how any test will perform in unselected populations. It therefore follows that such studies are largely unhelpful when looking at how diagnostic tests perform as a whole.

THE NEED FOR NEW GUIDELINES

Cardiovascular disease is the commonest cause of death in the western world and the diagnosis of chest pain is a major clinical and financial burden on healthcare systems.

The American Heart Association estimate cardiovascular disease costs the USA \$555 billion per annum and will rise to over \$1 Trillion dollars by 2035 assuming no management changes are made.⁶ Diagnostic testing is central in the diagnosis for the majority of patients and the use of both ICA and non-invasive tests has grown substantially with associated increasing expenditure.⁷ Until recently, most studies have compared different stress imaging modalities to detect obstructive CAD and have shown no definite evidence to recommend one diagnostic test over another.^{8,9} Functional testing has received criticism due to the high rate of false-positive results. Registry data have highlighted the low prevalence of obstructive CAD following ICA, despite prior stratification with functional testing to identify prognostically significant myocardial ischemia.¹⁰ This suggests that either current guidelines are not being adhered to or are not fit for purpose.

2010 NICE GUIDANCE

In the UK, the National Institute for Health and Care Excellence (NICE) reviews clinical evidence and publishes advice and recommendations based on the combination of clinical efficacy and cost-effectiveness of both therapies and technologies. In 2010¹ NICE made recommendations on the investigation of stable chest pain. These recommended eliciting a careful history of symptoms and estimating the pre-test likelihood (PTL) of significant CAD using a modified Diamond-Forrester model.⁴ Only patients with typical or atypical angina symptoms with a >10% PTL of obstructive CAD were recommended for investigation to confirm the diagnosis angina secondary to obstructive CAD. In patients with a PTL >90% a diagnosis of CAD was assumed clinically and ICA only performed in those who failed best medical management. If a patient's PTL was low (10–29%), a Coronary Artery Calcium Score was the recommended first-line investigation with subsequent CTCA if the calcium score was between 1 and 400 Agatston Units. If the PTL was intermediate (30–60%), non-invasive functional imaging was recommended, with ICA recommended for those with a high PTL (61–90%). Of note the use of the exercise ECG was no longer recommended because of its poor diagnostic performance in all patient groups.

The guidelines were largely greeted in a positive fashion and adherence to the guidelines was shown to be cost-effective.¹¹ However, concerns were quickly raised that the prevalence of CAD using the Diamond-Forrester model was being over estimated. The Diamond and Forrester disease estimates, and their modification in the Duke clinical score,¹² were developed more than 40 years ago when coronary disease was more prevalent and were derived from angiographic and autopsy populations, meaning that disease prevalence, upon which the estimates were based, was substantially higher than in contemporary populations. The exaggeration is substantial, the CONFIRM investigators reporting that the observed prevalence of significant (>50%) obstructive disease in 14,048 patients with suspected angina who underwent CTCA was only 18% compared with 51% predicted by the Diamond-Forrester disease estimates.¹³ For 70% stenosis the observed and predicted prevalence rates (10 vs 42%) showed even wider separation. Similar separation of observed and predicted rates of obstructive coronary disease

have been reported for the Duke clinical score, a modification of the Diamond-Forrester model recommended in the NICE 2010 guideline.¹⁴ False reassurance from atypical features, or a low risk score is also an issue. Under recognition of angina is associated with less aggressive treatment and greater risk.¹⁵ Such patients account for approximately a third of coronary deaths and non-fatal myocardial infarcts over the subsequent 5 years.¹⁶ This failure in both over estimation of disease and failure to identify patients at risk meant a review of their value was due.

Secondly the 2010 NICE review had, inevitably, reviewed the diagnostic accuracy of CTCA at a time when the technique, and the equipment was still in a stage of evolution. Early data had suggested that the accuracy of CTCA fell dramatically in the face of high calcium. Hence the suggestion that CTCA be abandoned if the calcium score was above 400. However, a subsequent NICE review in 2012 of New Generation scanners showed modern CT scanners could not only achieve high accuracy in the presence of high calcium (sensitivity 97.9, specificity 81.7%)¹⁷ but also in other difficult patient groups. Along with the improvements in diagnostic accuracy the radiation doses to patients during CTCA have fallen dramatically since the recommendations. A recent 50 centre UK audit showed the median DLP to be only 209 mGy cm⁻¹,¹⁸ which compares favourably to a similar 50 centre audit in 2009 of 888 mGy cm⁻¹.¹⁹ This reduction in patient risk, along with the overall improvements in diagnostic accuracy of CTCA and recognition of the falling prevalence of disease in the population all indicated to NICE that an update was required.

2016 UPDATE NICE GUIDANCE

As part of the NICE 2016 review an extensive literature review was performed of all diagnostic modalities in the general population presenting with chest pain using ICA as the gold standard as previously and is shown in Table 1. As can be seen established stress testing modalities all have comparable levels of diagnostic accuracy. In contrast CTCA has far higher sensitivity and as such the chance of missing significant disease was low, an important issue for the patient representatives on the committee. In addition to diagnostic accuracy of the tests estimates of the complications of the procedures and the costs of each procedure and of any complications are taken into account. The National Health Service (NHS) costs for the procedures in 2016 are shown in Table 2. Whilst one can argue the accuracy of such figures the counter argument is these are the actual figures agreed by Trusts and used by NHS organisations. Using these costings along with the accuracy of the tests, their complication rates, and the prevalence of disease, it is possible to perform economic modelling of all the diagnostic strategies in patients with differing levels of disease prevalence. For the sake of modelling ICA was assumed to be perfect in terms of accuracy. Despite the combination of its high cost and associated complication rate it failed to be the most cost-effective strategy in any population subgroup. In contrast CTCA with its low cost and superior accuracy, compared to other non-invasive functional tests, was found to be the most cost-effective diagnostic strategy in all patient subgroups. Of note economic modelling determined that only if the cost of cardiac CT tripled would it cease to be the least cost-effective initial investigation, and even then the next most cost-effective

Table 1. Meta analysis of diagnostic test accuracy NICE 2016

Test	Mean sensitivity	Low 95% confidence interval	High 95% confidence interval
Sensitivity			
ICA	1	n/a	n/a
CTCA	0.959	0.944	0.970
Echocardiography	0.756	0.720	0.789
Cardiac MRI	0.840	0.764	0.895
Single photon emission CT	0.806	0.735	0.861
Specificity			
ICA	1	n/a	n/a
CTCA	0.785	0.717	0.840
Echocardiography	0.804	0.706	0.876
Cardiac MRI	0.846	0.772	0.899
Single photon emission CT	0.784	0.698	0.852

CTCA, CT coronary angiography; ICA, invasive coronary angiography; NICE, National Institute for Health and Care Excellence.

strategy was a combination of CTCA with dobutamine stress echocardiography.²⁰

These findings allowed a significant shift in the diagnostic paradigm. As CTCA was the most effective diagnostic strategy in all population subgroups there is no longer a need for quantitative assessments of disease probability to determine the need for diagnostic testing and the choice of test. Instead, the recommendation is for no diagnostic testing if chest pain is judged to be “non-anginal” and computed CTCA in all patients with “typical” or “atypical” chest pain. Whilst this simplifies assessment it also places a greater emphasis on taking a good clinical assessment of symptoms to prevent overuse of investigation. Calcium scoring a routine procedure is no longer recommended as it adds radiation without increasing performance. Functional imaging is now only recommended in the context of non-anginal pain with abnormal ECG, if there is uncertainty about the functional significance of coronary lesions or CTCA is non-diagnostic. Even in this scenario the results must be considered in the

appropriate clinical context. It is imperative to remember a negative functional test does not rule out coronary atherosclerosis or non-obstructive CAD. In fact, a negative functional test does not rule out obstructive CAD as the sensitivity of functional testing is imperfect. Indeed, modelling exercises by NICE indicated that the use of a Functional test following a diagnostic CTCA as a routine resulted in greater patient misclassification than CTCA alone.

Not only have new NICE guidelines simplified the diagnostic pathway, but such changes will also save significant amounts of money. NICE has calculated that the use of CTCA as a first-line investigation will generate annual savings of £16 million in England alone, by prompt exclusion of significant CAD and more effective use of resources.²¹

CHALLENGES TO THE IMPLEMENTATION OF THE 2016 NICE GUIDELINES

The publication of the 2016 guidelines represents a major shift in the diagnostic paradigm with significant cost savings and benefits to patients. In so doing however it creates a number of major challenges. Firstly, a massive increase in the availability of CTCA is required. An estimate by the British Society of Cardiovascular Imaging/British Society of Cardiovascular CT is that a 700% increase in cardiac CT will be required in the UK.²² In order to achieve this service requirement, substantial investment in CT scanners will be required. The UK has a relatively low number of CT scanners per head of population compared to other countries in Europe and the USA and as such the service cannot be delivered on the existing UK CT base.²³

Secondly, it is essential that the quality of CTCA reporting is high in order to replicate trial data of the high diagnostic accuracy of CTCA. This includes optimisation of image quality and radiation exposure. Guidelines for the optimal acquisition of cardiac CT have been published and should be followed.²² Training in such techniques and the reporting of such scans also represents a problem and will require a coordinated response from Royal Colleges and specialist interest groups. Guidelines are available for the structured reporting of cardiac CT, which may help new reporters communicate results.²⁴ It is also important that the temptation to confirm the CTCA finding with ICA is avoided. This will increase not only costs but also expose patients to increased radiation and risk with marginal benefit.

Table 2. NHS costings used by NICE 2016

Test	Code, description	Source	Amount
ICA	EY43A to EY43F, standard cardiac catheterisation	NHS reference costs 2014–15, weighted average	£1684.71
CTCA	RD28Z, complex computerised tomography scan	NHS reference costs 2014–15	£122.11
Single photon emission CT	RN21Z, myocardial perfusion scan, stress only	NHS reference costs 2014–15	£367.29
Echocardiography	EY50Z, complex echocardiogram	NHS reference costs 2014–15	£271.31
Cardiac magnetic resonance	RA67Z, cardiac magnetic imaging scan, pre and post contrast	Enhanced tariff option 2015–16	£515.00

CTCA, CT coronary angiography; ICA, invasive coronary angiography; NHS, National Health Service; NICE, National Institute for Health and Care Excellence.

Thirdly, there will be implications for functional imaging modalities. Whilst second line testing will be required in some patients realistically requirements will reduce. In addition, the introduction of Recent NICE-approved software developments has extended the functionality of CTCA by providing a non-invasive method of estimating FFRCT using standard CTCA imaging data.²⁵ FFRCT in a post processing tool that allows estimation of the haemodynamic significance of a stenosis using computational fluid dynamics on standard DICOM data.²⁶ In the recent PLATFORM study, patients in the CTCA cohort who underwent simultaneous estimation of FFRCT showed dramatic reductions to 12% in the rate of normal coronary angiography compared with 73% in the standard care cohort, emphasizing the potential value of combined anatomical and functional assessments that

CTCA now offers.²⁷ The exact role for functional testing is therefore uncertain and will require ongoing critical evaluation.

CONCLUSION

The 2016 update to the NICE chest pain guideline marks a radical departure from the previous version that should be welcomed. No longer is there a need to apply probability estimates of CAD in order to guide decisions about non-invasive diagnostic testing. Instead, the new recommendation is for CTCA in all patients with typical or atypical chest pain to be based on the diagnostic accuracy and cost-effectiveness of this strategy. The implementation of these guidelines requires a large increase in the number of CT scans that are performed; however, the projected cost savings mean that the short-term investment is justified.

REFERENCES

1. Bourassa MG. The history of cardiac catheterization. *Can J Cardiol* 2005; **21**: 1011–4.
2. National Institute for Health and Care Excellence. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. NICE guidelines [CG95]. 2010. Available from: <https://www.nice.org.uk/guidance/cg95/resources/guidance-chest-pain-of-recent-onset>.
3. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013; **34**: 2949–3003. doi: <https://doi.org/10.1093/eurheartj/ehd296>
4. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012; **60**: e44–e164. doi: <https://doi.org/10.1016/j.jacc.2012.07.013>
5. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med* 1979; **300**: 1350–8. doi: <https://doi.org/10.1056/NEJM197906143002402>
6. American Heart Association. Cardiovascular disease costs will exceed \$1 trillion by 2035, warns the American Heart Association. 2017. Available from: http://www.heart.org/adc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_491543.pdf.
7. Lucas FL, DeLorenzo MA, Siewers AE, Wennberg DE. Temporal trends in the utilization of diagnostic testing and treatments for cardiovascular disease in the United States, 1993–2001. *Circulation* 2006; **113**: 374–9. doi: <https://doi.org/10.1161/CIRCULATIONAHA.105.560433>
8. Greenwood JP, Ripley DP, Berry C, McCann GP, Plein S, Bucciarelli-Ducci C, et al. Effect of care guided by cardiovascular magnetic resonance, myocardial perfusion scintigraphy, or NICE guidelines on subsequent unnecessary angiography rates: the CE-MARC 2 randomized clinical trial. *JAMA* 2016; **316**: 1051–60. doi: <https://doi.org/10.1001/jama.2016.12680>
9. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 2015; **372**: 1291–300. doi: <https://doi.org/10.1056/NEJMoa1415516>
10. 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. doi: <https://doi.org/10.1056/NEJMoa0907272>
11. Lee AJ, Michail M, Quaderi SA, Richardson JA, Aggarwal SK, Speechly-Dick ME. Implementation of NICE clinical guideline 95 for assessment of stable chest pain in a rapid access chest pain clinic reduces the mean number of investigations and cost per patient. *Open Heart* 2015; **2**: e000151. doi: <https://doi.org/10.1136/openhrt-2014-000151>
12. Pryor DB, Shaw L, McCants CB, Lee KL, Mark DB, Harrell FE, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med* 1993; **118**: 81–90. doi: <https://doi.org/10.7326/0003-4819-118-2-199301150-00001>
13. Cheng VY, Berman DS, Rozanski A, Dunning AM, Achenbach S, Al-Mallah M, et al. 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**: 2423–32. doi: <https://doi.org/10.1161/CIRCULATIONAHA.111.039255>
14. Genders TS, Steyerberg EW, Hunink MG, Nieman K, Galema TW, Mollet NR, et al. Prediction model to estimate presence of coronary artery disease: retrospective pooled analysis of existing cohorts. *BMJ* 2012; **344**: e3485. doi: <https://doi.org/10.1136/bmj.e3485>
15. Qintar M, Spertus JA, Gosch KL, Beltrame J, Kureshi F, Shafiq A, et al. Effect of angina under-recognition on treatment in outpatients with stable ischaemic heart disease. *Eur Heart J Qual Care Clin Outcomes* 2016; **2**: 208–14. doi: <https://doi.org/10.1093/ehjqcco/qcw016>
16. Sekhri N, Feder GS, Junghans C, Hemingway H, Timmis AD. How effective are rapid

- access chest pain clinics? Prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients. *Heart* 2007; **93**: 458–63. doi: <https://doi.org/10.1136/hrt.2006.090894>
17. National Institute for Health and Care Excellence. New generation cardiac CT scanners (Aquilion ONE, Brilliance iCT, Discovery CT750 HD and Somatom Definition Flash) for cardiac imaging in people with suspected or known coronary artery disease in whom imaging is difficult with earlier generation CT scanners. 2012. Available from: <https://www.nice.org.uk/guidance/dg3>.
 18. Castellano IA, Nicol ED, Bull RK, Roobottom CA, Williams MC, Harden SP. A prospective national survey of coronary CT angiography radiation doses in the United Kingdom. *J Cardiovasc Comput Tomogr* 2017; **11**: 268–73. doi: <https://doi.org/10.1016/j.jcct.2017.05.002>
 19. Hausleiter J, Meyer T, Hermann F, Hadamitzky M, Krebs M, Gerber TC, et al. Estimated radiation dose associated with cardiac CT angiography. *JAMA* 2009; **301**: 500–7. doi: <https://doi.org/10.1001/jama.2009.54>
 20. National Institute for Health and Care Excellence. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. NICE guidelines [CG95]. 2016. Available from: <https://www.nice.org.uk/guidance/cg95>.
 21. National Institute for Health and Care Excellence. Putting NICE Guidance into Practice. Resource impact report: chest pain of recent onset: assessment and diagnosis. 2016. Available from: <https://www.nice.org.uk/guidance/cg95/resources/resource-impact-report-2726121709>.
 22. Nicol E, Padley S, Roditi G, Roobottom C. The challenge of national CT coronary angiography (CTCA) provision in response to NICE CG95. 2016. Available from: http://www.bsci.org.uk/images/Documents/2016_BSCI_BSCCT_response_to_NICE_CG95.pdf.
 23. OECD. OECD health statistics 2014 - frequently requested data. 2014. Available from: <http://www.oecd.org/els/health-systems/oecd-health-statistics-2014-frequently-requested-data.htm>.
 24. Cury RC, Abbara S, Achenbach S, Agatston A, Berman DS, Budoff MJ, et al. CAD-RADS™ coronary artery disease - reporting and data system. An expert consensus document of the society of cardiovascular computed tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NASCI). Endorsed by the American College of Cardiology. *J Cardiovasc Comput Tomogr* 2016; **10**: 269–81. doi: <https://doi.org/10.1016/j.jcct.2016.04.005>
 25. National Institute for Health and Care Excellence. HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography. NICE Medical technologies guidance [MTG32]. 2017. Available from: <https://www.nice.org.uk/guidance/mtg32> [Published date: February 2017].
 26. Pang CL, Alcock R, Pilkington N, Reis T, Roobottom C. Determining the haemodynamic significance of arterial stenosis: the relationship between CT angiography, computational fluid dynamics, and non-invasive fractional flow reserve. *Clin Radiol* 2016; **71**: 750–7. doi: <https://doi.org/10.1016/j.crad.2016.03.001>
 27. Douglas PS, Pontone G, Hlatky MA, Patel MR, Norgaard BL, Byrne RA, et al. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFR(CT): outcome and resource impacts study. *Eur Heart J* 2015; **36**: 3359–67. doi: <https://doi.org/10.1093/eurheartj/ehv444>