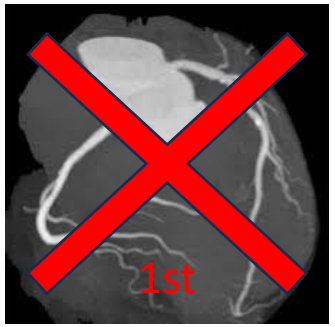
Η Αξονική Στεφανιογραφία πρέπει να είναι το εργαλείο απεικόνισης πρώτης γραμμής για τη διάγνωση της στεφανιαίας νόσου

ΚΑΤΑ



Ματθαίος Β. Διδάγγελος

Επεμβατικός Καρδιολόγος, Επιμ. Β΄ Ε.Σ.Υ.

Α' Πανεπιστημιακή Καρδιολογική Κλινική Α.Π.Θ., Π.Γ.Ν.Θ. ΑΧΕΠΑ

Conflicts of interest

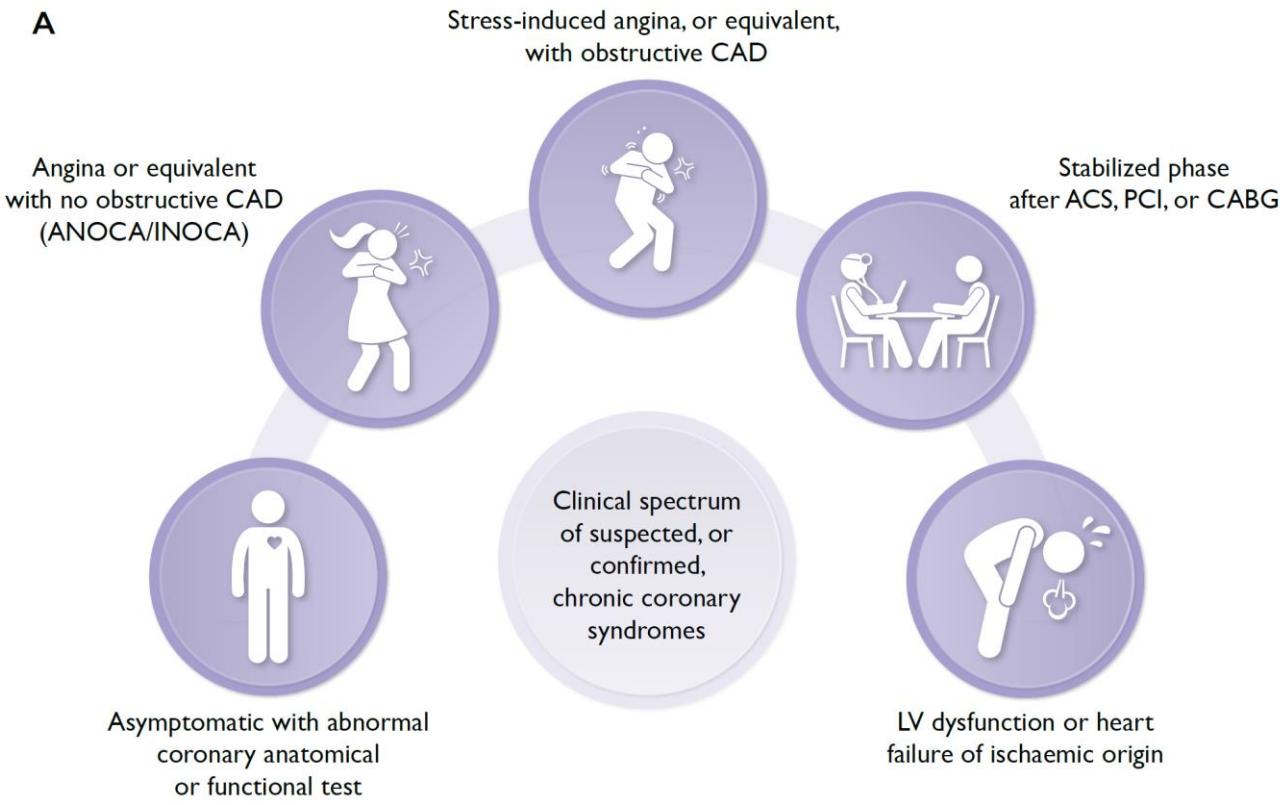
- None

CTCA in CAD imaging

- CCS
- ACS

Chronic Coronary Syndromes

- The initial evaluation of stable chest pain patients should be:
  - practical
  - safe
  - cost-effective
  - accurate in diagnosing aetiology
  - effective in guiding therapy



PROMISE trial

- 10,003 symptomatic patients – stable angina or equivalents
  - mean pretest likelihood of obstructive CAD: 53.3±21.4%

- Randomized to:
  - CTCA or
  - functional testing (exercise ECG, nuclear stress testing, or stress echo)

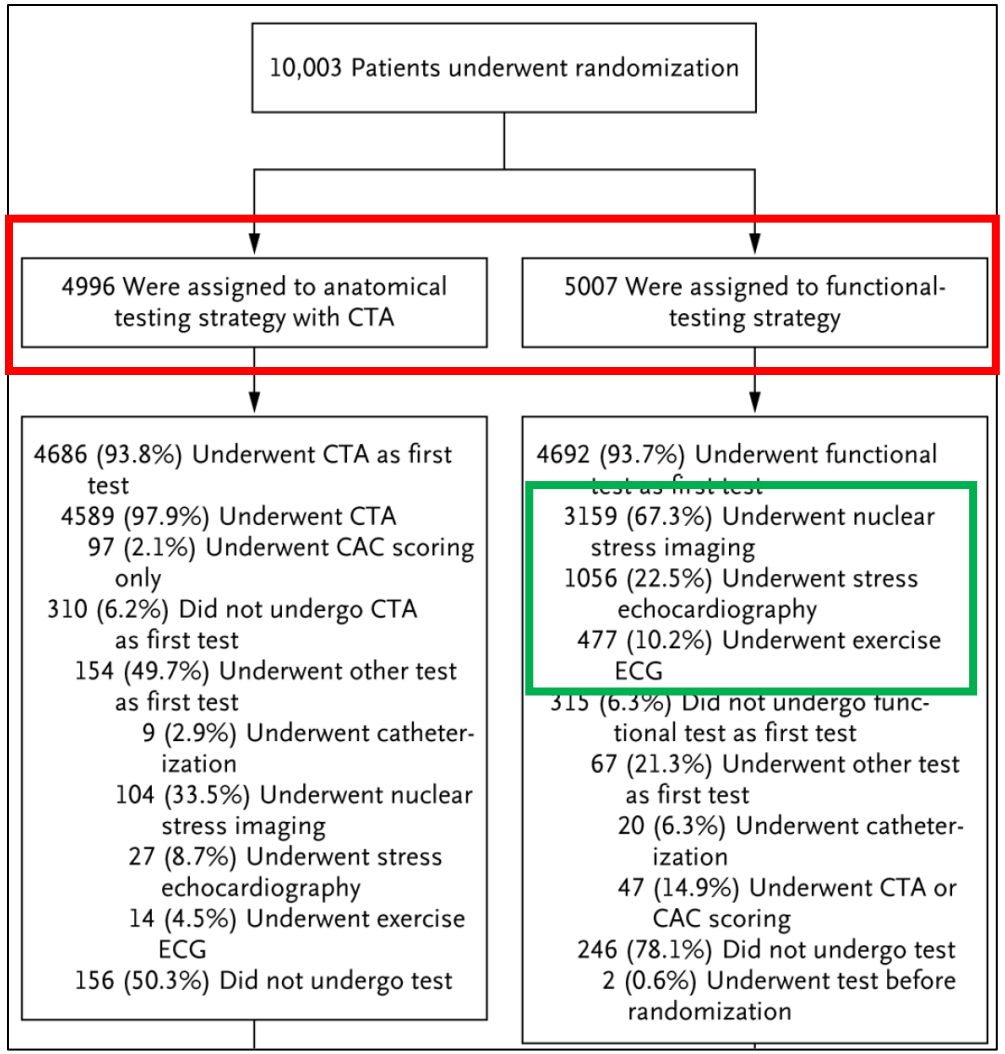
- Primary end point:
  - death, myocardial infarction, hospitalization for unstable angina, or major procedural complication

- Secondary end points:
  - invasive cardiac catheterization that did not show obstructive CAD
  - radiation exposure

- FU: 2 years

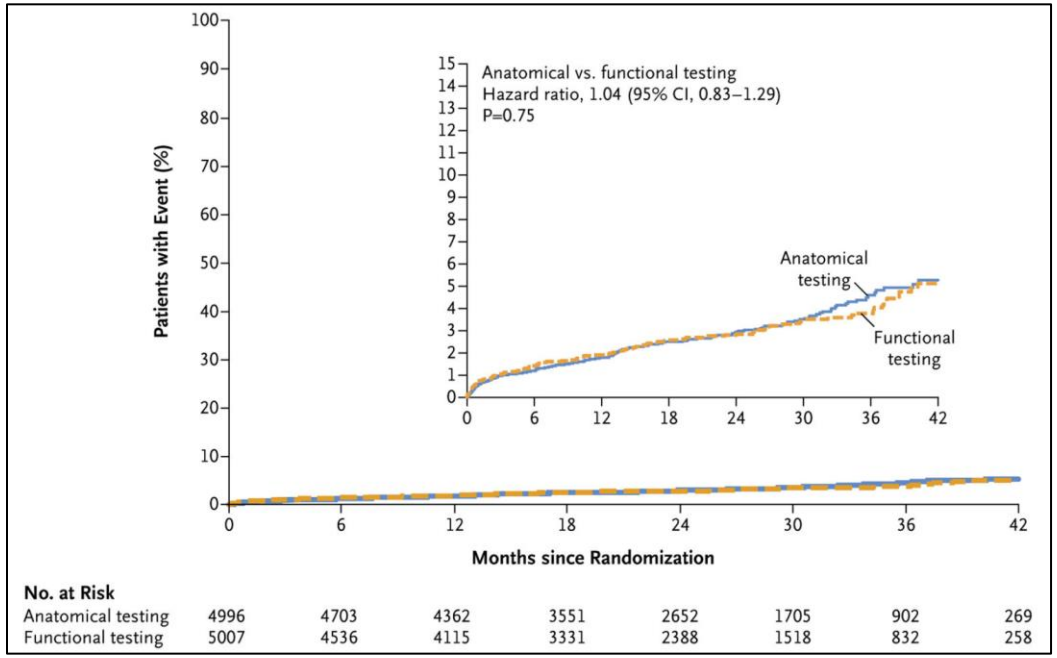
Douglas PS, et al. PROMISE trial. N Engl J Med. 2015;372(14):1291-300.

PROMISE trial - Flowchart



Douglas PS, et al. PROMISE trial. N Engl J Med. 2015;372(14):1291-300.

PROMISE trial - Results



End Point	CTA Strategy (N = 4996)	Functional-Testing Strategy (N = 5007)	Adjusted Hazard Ratio (95% CI)	P Value
Clinical end point — no. of patients				
Primary composite end point	164	151	1.04 (0.83–1.29)	0.75
Death from any cause	74	75		
Nonfatal myocardial infarction	30	40		
Hospitalization for unstable angina	61	41		
Major procedural complication	4	5		
Primary end point plus catheterization showing no obstructive CAD	332	353	0.91 (0.78–1.06)	0.22
Death or nonfatal myocardial infarction	104	112	0.88 (0.67–1.15)	0.35
Death, nonfatal myocardial infarction, or hospitalization for unstable angina	162	148	1.04 (0.84–1.31)	0.70
Test-related end point				
Invasive catheterization showing no obstructive CAD — no. (%)	170 (3.4)	213 (4.3)	—	0.02
Cumulative radiation exposure in all procedures ≤90 days after randomization — mSv				
All patients	12.0±8.5	10.1±9.0	—	<0.001

- CTCA
  - did not reduce the composite primary endpoint
  - higher 90-day referral rate to invasive coronary angiography (ICA) (12.2% vs. 8.1%)
  - higher coronary revascularization (6.2% vs. 3.2%)
  - higher overall exposure to medical radiation

Douglas PS, et al. PROMISE trial. N Engl J Med. 2015;372(14):1291-300.

SCOT-HEART trial

- 4146 patients with stable chest pain

- Randomized to:
  - standard care plus CTCA or
  - standard care alone (routine clinical evaluation, including, if deemed appropriate, symptom limited exercise ECG, stress imaging or invasive coronary angiography)

- Primary end point:
  - death from coronary heart disease or nonfatal myocardial infarction

- FU: 5 years

Newby DE, et al. SCOT-HEART Investigators. N Engl J Med. 2018;379(10):924-933.

SCOT-HEART trial - Results

Table 2. Primary and Secondary End Points after a Median Follow-up of 4.8 Years.*

End Point	All Participants (N=4146)	Standard Care (N=2073)	Standard Care plus CTA (N=2073)	Hazard Ratio (95% CI)†
	number of patients (percent)			
Primary end point: death from CHD or non-fatal myocardial infarction‡	129 (3.1)	81 (3.9)	48 (2.3)	0.59 (0.41–0.84)§
Secondary end points				
Death from CHD, nonfatal myocardial infarction, or nonfatal stroke‡	160 (3.9)	97 (4.7)	63 (3.0)	0.65 (0.47–0.89)
Nonfatal myocardial infarction	117 (2.8)	73 (3.5)	44 (2.1)	0.60 (0.41–0.87)
Nonfatal stroke	35 (0.8)	20 (1.0)	15 (0.7)	0.74 (0.38–1.44)
Death				
From CHD‡	13 (0.3)	9 (0.4)	4 (0.2)	0.46 (0.14–1.48)
From any cause	86 (2.1)	43 (2.1)	43 (2.1)	1.02 (0.67–1.55)
Cardiovascular	17 (0.4)	12 (0.6)	5 (0.2)	0.43 (0.15–1.22)
Noncardiovascular	69 (1.7)	31 (1.5)	38 (1.8)	1.24 (0.77–2.00)
Procedures				
Invasive coronary angiography	993 (24.0)	502 (24.2)	491 (23.7)	1.00 (0.88–1.13)
Revascularization¶	546 (13.2)	267 (12.9)	279 (13.5)	1.07 (0.91–1.27)
Percutaneous coronary intervention	431 (10.4)	212 (10.2)	219 (10.6)	1.06 (0.88–1.28)
Coronary-artery bypass grafting	131 (3.2)	62 (3.0)	69 (3.3)	1.12 (0.80–1.58)

- CTCA
  - reduction of non-fatal MI at 5 years despite initially demonstrating no difference in outcomes (probably due to improved medical treatment in CTCA arm)
  - No less ICA
  - No less revascularization

Newby DE, et al. SCOT-HEART Investigators. N Engl J Med. 2018;379(10):924-933.

Table 1 Key limitations of the SCOT-HEART and PROMISE trials

No.	Trial limitations	Impact
SCOT-HEART		
1.	Layered strategy combining anatomical CTCA data and functional ETT data instead of only early CTCA	Trial does not explore role of CTCA as first strategy but rather the role of the layered strategy
2.	Low use of functional testing	Not representative of standard of care in most centres
3.	No pre-specified guiding protocols for CTCA in both trial arms	Unclear explanation of how CTCA improved medical therapy over ETT alone
4.	Concern of patients treated sub-optimally in the standard care arm	Risk of bias against standard care arm
5.	Long-term outcome data only extracted from electronic records with no formal event adjudication	Risk of bias as potential outcome events were not evaluated by independent and blinded experts
6.	Pre-specified cost-effectiveness analysis not yet published	Cost-effectiveness of CTCA in the trial unknown
PROMISE		
1.	Ratio of functional testing strategies was focused more on reflecting current practice conditions in trial sites	Trial does not provide definitive insight into the harm or benefits of CTCA compared with functional testing
2.	More advanced functional methods such as PET or CMR were either under-represented or not used	Low or no representation of PET or CMR, and the lack of imaging in ETT (10%) may have caused bias against the functional testing arm
3.	Study does not explore test utility or performance	Utility and performance values of testing strategies unknown

Berry C, et al. Eur Heart J. 2023;44(26):2366-2375.

Risk category into consideration

- PROMISE and SCOT-HEART trials studied low or low-intermediate risk patients
- Indeed, demonstrated that CTCA is useful in ruling out CAD in patients from these pre-test risk groups
- However, anatomical CTCA does not perform as robustly in ruling out CAD in intermediate-high risk symptomatic patients
- Given the prevalence of obstructive CAD in symptomatic chest pain patients is generally low (<10%) → anatomical imaging by a CTCA-first strategy has a lower test specificity for significant stenosis that warrants coronary intervention, in comparison with most non-invasive functioning tests

Juarez-Orozco LE, et al. Eur Heart J Cardiovasc Imaging 2019;20:1198–1207.

CE-MARC2 trial

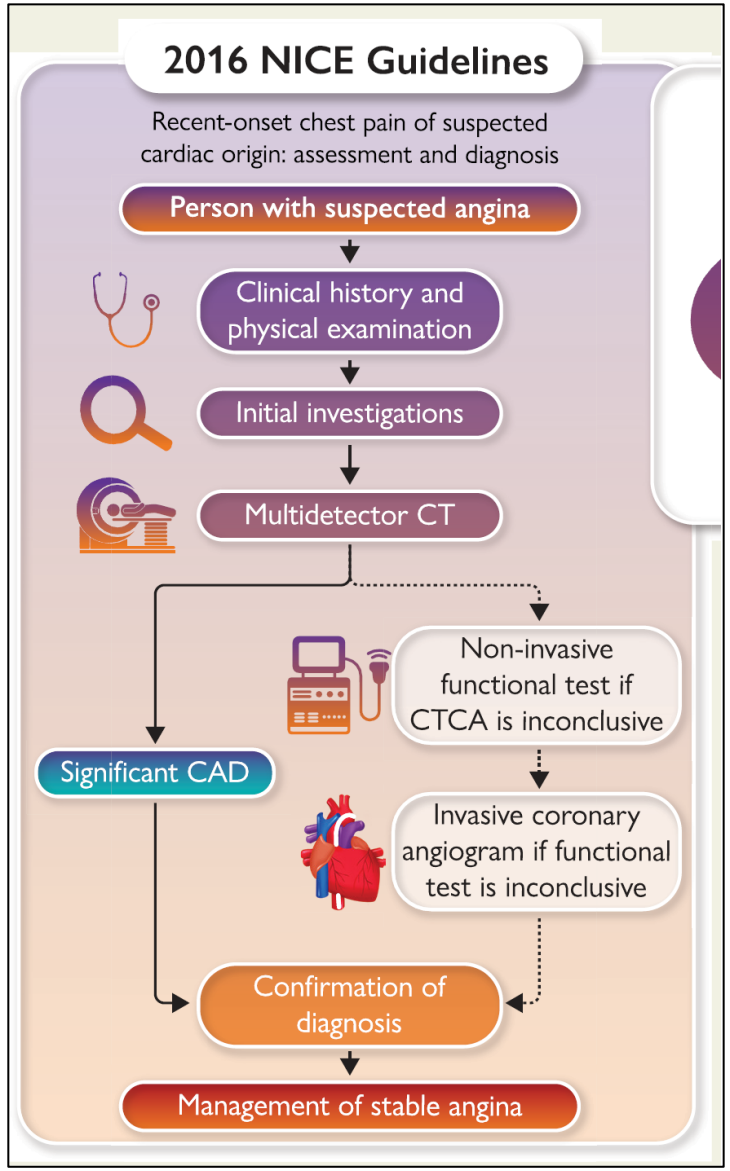
- 1202 symptomatic patients - stable angina
  - Pretest likelihood of 10%-90%

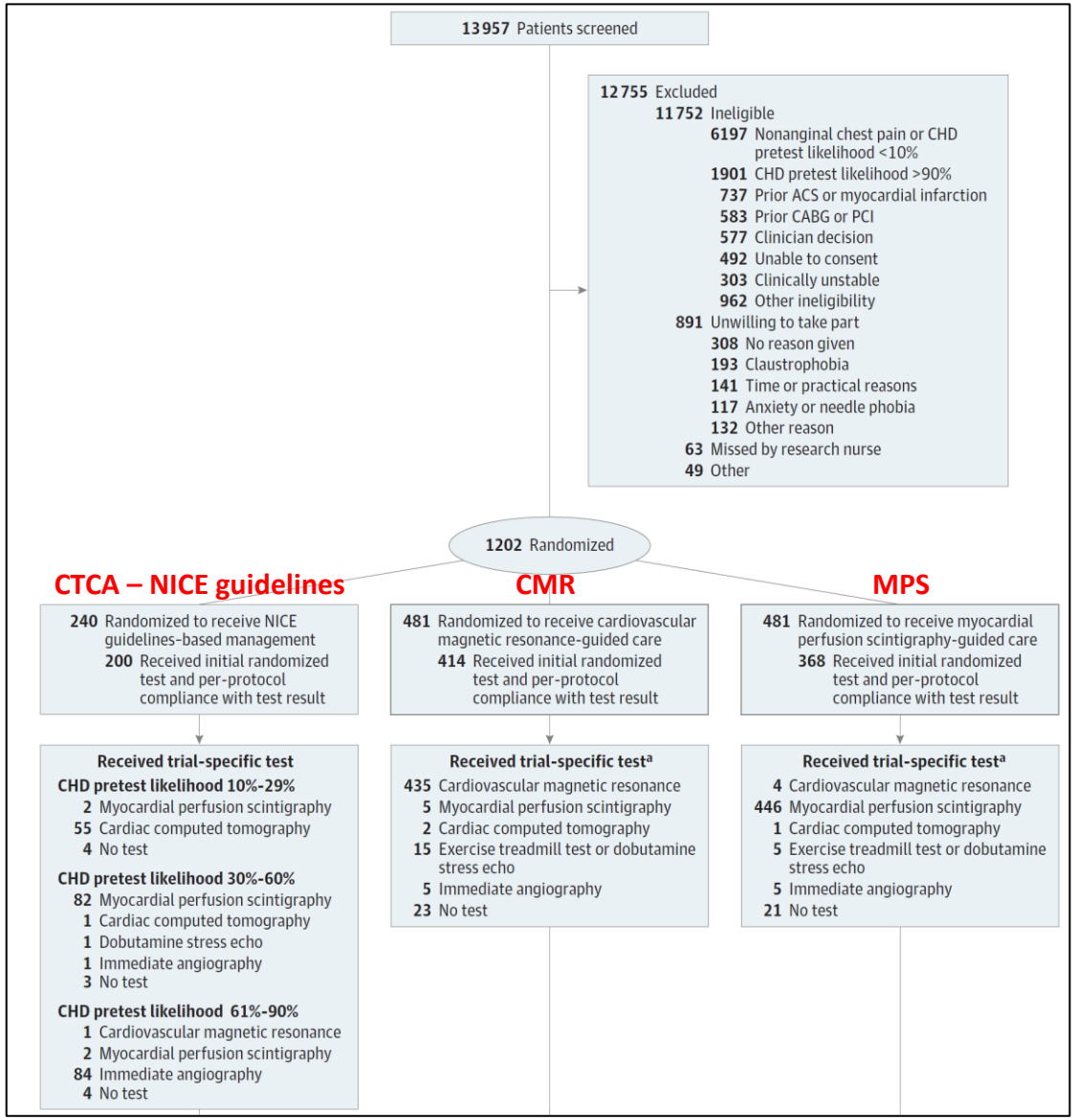
- Primary endpoint (12m)
  - unnecessary coronary angiography

- Secondary end points (12m)
  - positive angiography
  - MACEs
  - procedural complications

Greenwood JP, et al. CE-MARC 2 Investigators. JAMA. 2016;316(10):1051-60.

CE-MARC2 trial





Greenwood JP, et al. CE-MARC 2 Investigators. JAMA. 2016;316(10):1051-60.

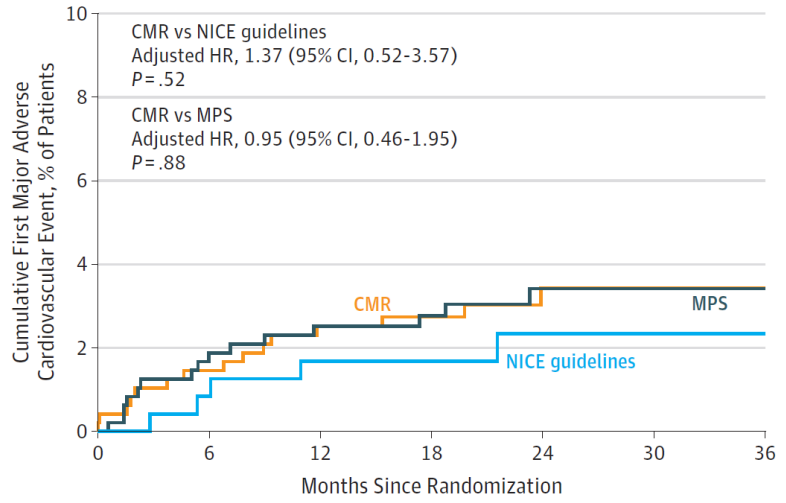
CE-MARC2 trial

Table 2. Summary of Trial End Points for Patients With Suspected Coronary Heart Disease, by Each Guided Care Group

		Guided Care			Absolute Differences, % (95% CI)	
	Total Patients (N = 1202)	NICE Guidelines (n = 240)	CMR (n = 481)	MPS (n = 481)	CMR vs NICE	CMR vs MPS
Primary End Point						
Unnecessary invasive angiography, No. of patients (%)	139 (11.6)	69 (28.8)	36 (7.5)	34 (7.1)	−21.3 (−28.7 to −13.6)	0.4 (−6.0 to 6.8)
Components of the primary end point						
False-positive noninvasive test	35	5	18	12		
Direct to angiography (by strategy)	59	59				
Negative noninvasive test, not per-protocol	41	5	15	21		
Inconclusive noninvasive test or result	4		3	1		

- CTCA
  - more unnecessary ICA
- CMR=MPS for ICA
- CTCA=CMR=MPS for MACE

Figure 3. Time to First Major Adverse Cardiovascular Event After a Minimum of 12-Month Follow-up From Randomization Among Patients With Suspected Coronary Heart Disease (Median, 16 Months)



Greenwood JP, et al. CE-MARC 2 Investigators. JAMA. 2016;316(10):1051-60.

openheart

Downstream testing after CT coronary angiography: time for a rethink?

Gareth Morgan-Hughes ,[1] Michelle Claire Williams ,[2,3] Margaret Loudon ,[1] Carl A Roobottom,[4] Alice Veitch,[5] Robin Van Lingen,[6] Ben Holloway,[7] Nicholas Bellenger,[8] Matthias Schmitt,[9] Russel Bull[10]

- Prospective UK registry on CTCA use in stable CAD
- 5293 patients

Morgan-Hughes G, et al. Open Heart. 2021;8(1):e001597.

openheart

Downstream testing after CT coronary angiography: time for a rethink?

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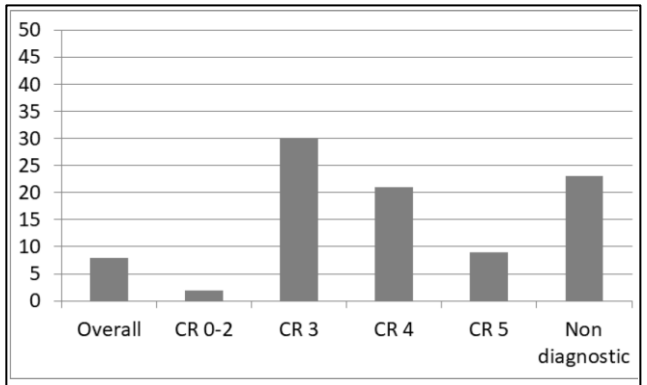


Figure 2 Patients (%) undergoing functional testing* after all CT coronary angiography by Coronary Artery Disease–Reporting and Data System (CR) score. *Includes patients undergoing functional testing as a third-line investigation after invasive coronary angiography had been used as a second-line investigation.

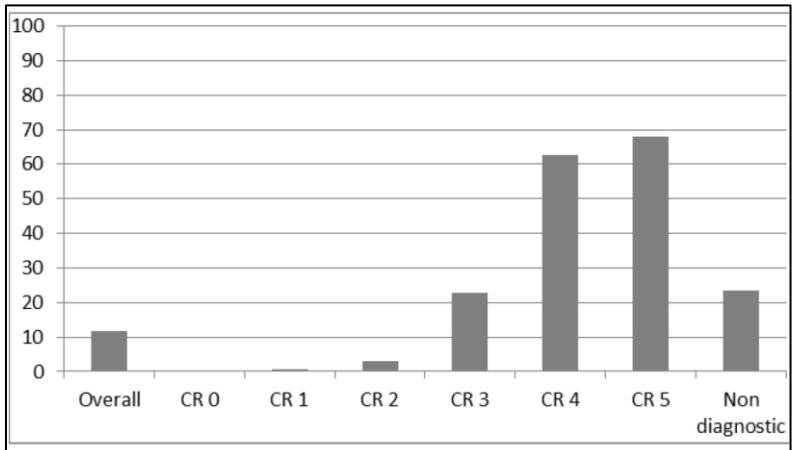


Figure 3 Invasive coronary angiography rates (%) after all CT coronary angiography by Coronary Artery Disease–Reporting and Data System (CR) score

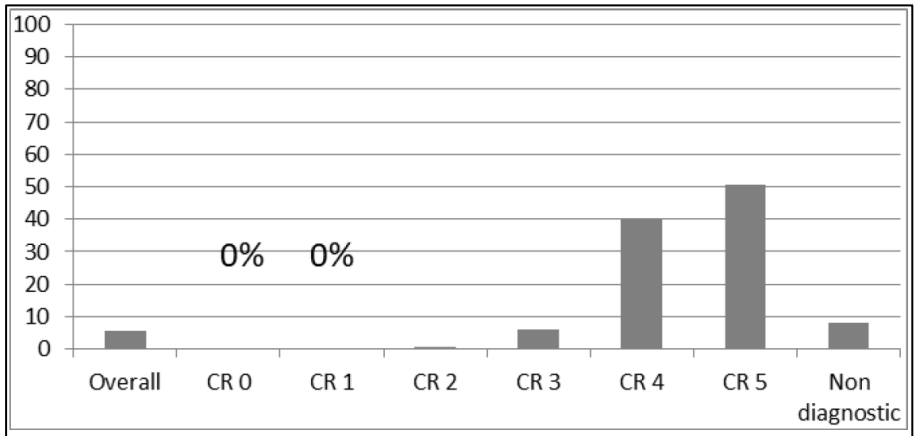


Figure 4 Revascularisation rates after all CT coronary angiography by Coronary Artery Disease–Reporting and Data System (CR) score (%).

CTCA negates the need for **further investigation in 73%** of patients

CTCA leads to **12% ICA → 48% overuse** (not receiving revascularization)

Morgan-Hughes G, et al. Open Heart. 2021;8(1):e001597.

What about FFR-CT?

- FFR-CT could integrate anatomy and luminal physiology as a ‘one-stop-shop’ to guide ICA referral

- However, FFR-CT quantitation has significant limitations:
  - involves assumptions in its fluid dynamics computational models
  - requires artefact-free imaging
  - is not robust in patients with atrial fibrillation, prior coronary stenting or extensive coronary calcification, severe valvular heart disease, sequential luminal lesions, or prior coronary bypass

- 20%-40% of CTCA studies may be deemed inadequate for FFR-CT analysis

Berry C, et al. Eur Heart J. 2023;44(26):2366-2375.

What about FFR-CT?

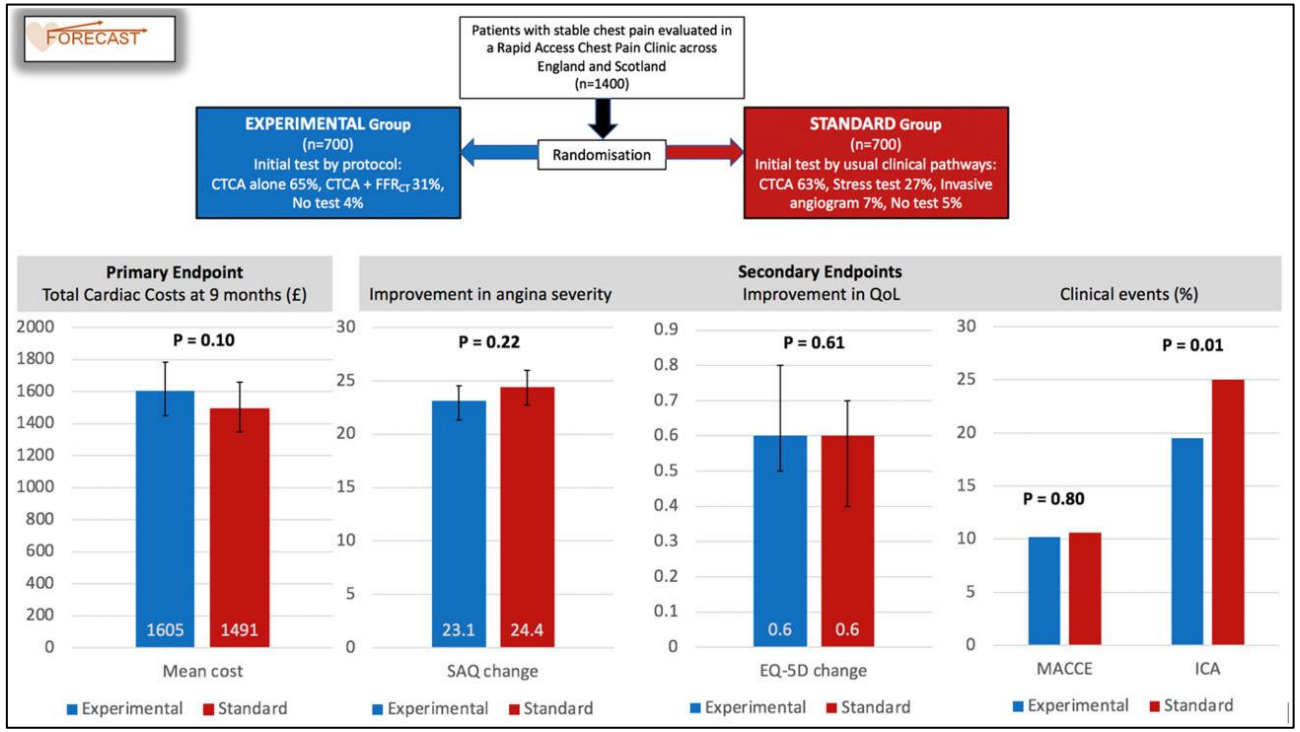
- Correlation of FFR-CT with invasive FFR is not high in contrast with the established evidence by functional imaging such as CMR or PET
  - In a meta-analysis using invasive FFR as the reference standard, an FFR-CT cut-off of 0.73 only achieved a 50% per-vessel agreement with invasive FFR. When a diagnostic threshold of 95% was set, only FFR-CT values measured to be in the extreme ends (below 0.53 or above 0.93) met this threshold

- Clinical adaptation and prognostic implications of FFR-CT are both substantially more limited than any one of the conventional functional imaging methods
  - Logistically, the only approved method at present is an off-site solution offered by a commercial vendor (HeartFlow, Redwood City, CA, USA) at approximately £530 (~620 Euros) per analysis in addition to the £220 (~258 Euros) per NHS cost of the CTCA scan

Cook CM, et al. JAMA Cardiol 2017;2:803–810.

FORECAST trial

- 1400 patients - stable angina
- Randomization FFR-CT vs standard care
- FFR-CT guided care did not result in benefits in healthcare costs, cardiovascular outcomes, or quality of life
- FFR-CT did reduce the use of ICA but the comparative group was primarily CTCA itself, not functional imaging



Curzen N, et al. Eur Heart J. 2021;42(37):3844-3852.

Table 2 Technical factors affecting role of CTCA as a widespread first-line test

No.	CTCA technical limitations
1.	Non-diagnostic studies due to extensive coronary calcification in older and diabetic patients
2.	Risk of nephrotoxicity from iodinated contrast media
3.	Lower resolution for small vessel calibres and inability to assess microvasculature
4.	Artefacts from previous stents, sternal wires from CABG, and other metallic implanted devices
5.	Exposure to ionizing radiation
6.	Limited availability of CTCA capable scanners and certified practitioners globally

Other functional testing VS CTCA

Table 3 Functional testing vs. CTCA

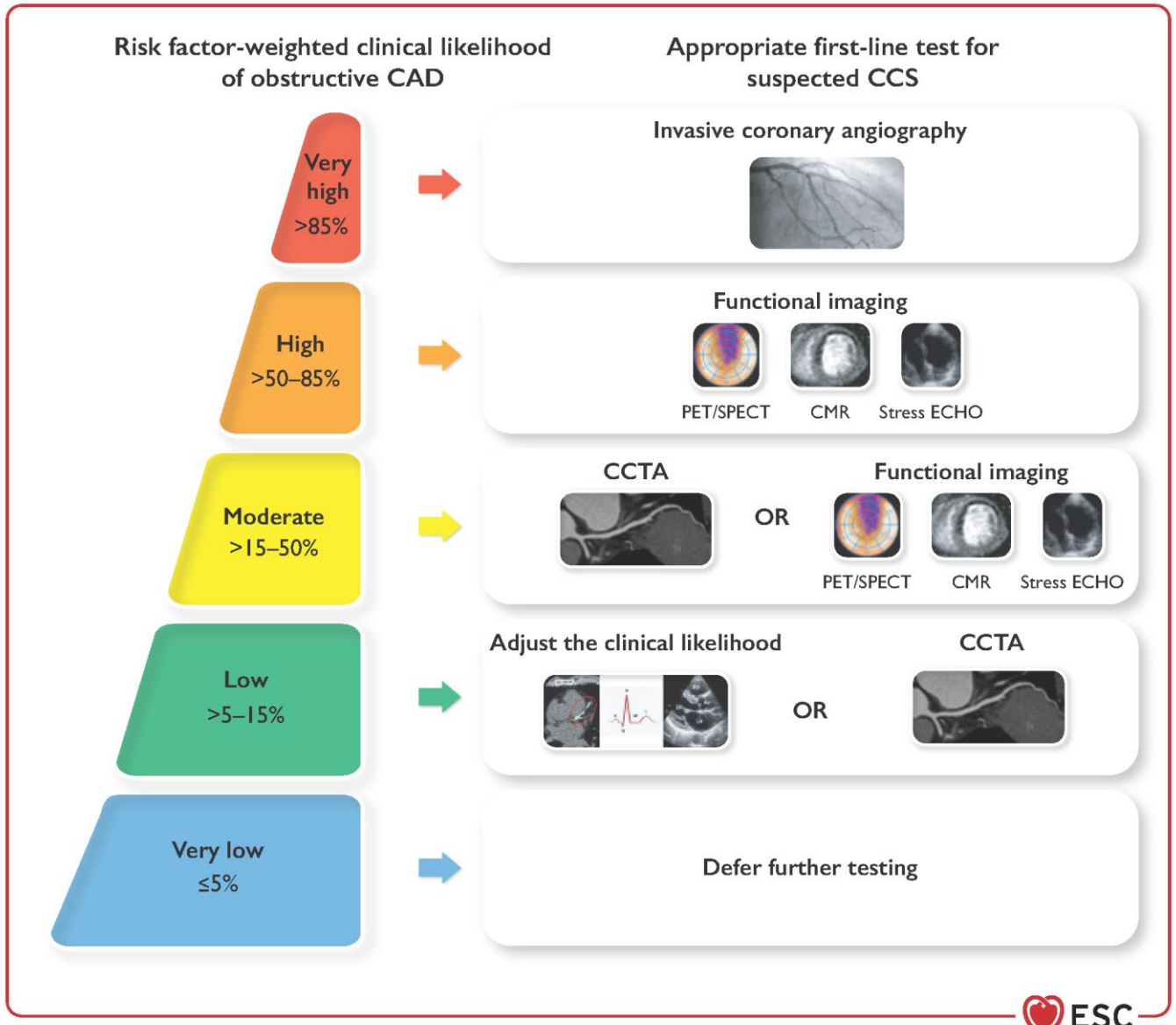
Functional	CTCA
In diagnosis of symptom aetiology	
• Higher test specificity for CAD	• Lower test specificity for CAD
• Excellent in assessing microvascular causes (INOCA, MINOCA)	• Limited ability to assess microvascular or vasospastic causes (INOCA, MINOCA)
• Capable of detecting pericardial and myocardial inflammatory diseases	• Less sensitive to detecting pericardial and myocardial inflammatory diseases
• Reliable in patients with extensive calcification, previous coronary stenting, CABG, and implanted devices	• Less robust in patients with extensive calcification, previous coronary stenting, CABG, and implanted devices
In predicting prognosis	
• Extensive prognostic evidence by the extents of ischaemic burden and viability to assess risk of adverse outcomes	• Extremely low patient risk of serious heart events if normal CTCA, but risk is variable in abnormal CTCA
In guiding intervention	
• Less associated with unnecessary ICA	• Associated with an overuse of ICA, which is important in the current era of decreasing CAD prevalence
• All functional modalities have reasonable clinical adaptation in guiding intervention	• FFR_{CT} is not well adapted clinically, costly, and with limited evidence in effective guidance of intervention
• Able to detect and size the extents of ischaemic burden and viability to guide invasive coronary referral	• Not able to detect size and extent of ischaemia and myocardial viability to guide further invasive coronary referral

2024 ESC Guidelines for the management of chronic coronary syndromes

2024 ESC Guidelines for the management of chronic coronary syndromes
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

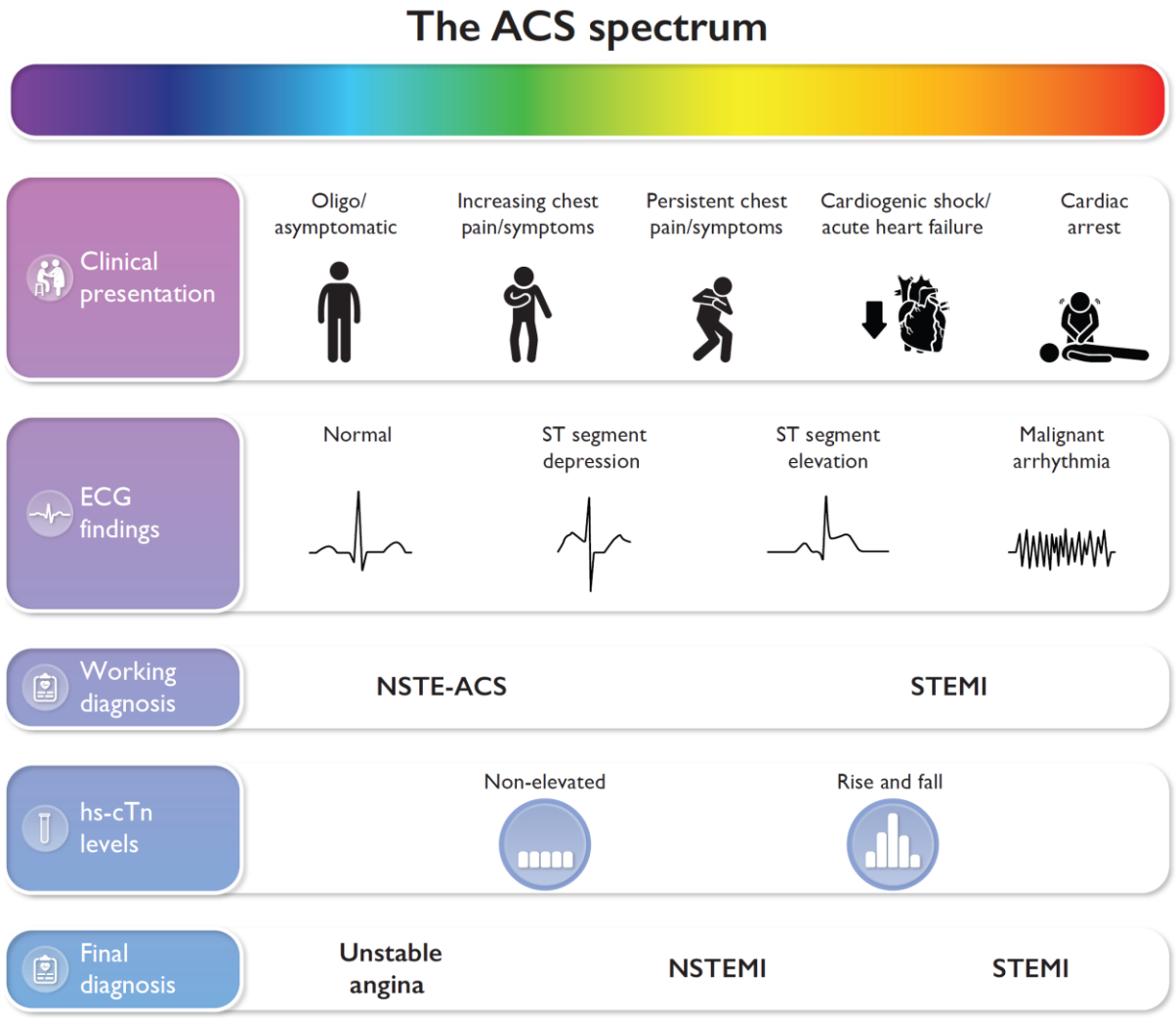
Figure 6

Appropriate first-line testing in symptomatic patients with suspected CCS



2024 ESC Guidelines for the management of chronic coronary syndromes
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae177)

Acute Coronary Syndromes



CTCA in ACS

- Generally, CT does not have a role in patients presenting with suspicion of ongoing acute coronary occlusion, for whom emergency ICA is the priority

- CT is often the diagnostic tool of choice for ruling out alternative potentially life-threatening differential diagnoses of ACS
  - PE
  - aortic dissection

- Many trials in NSTE-ACS (all negative for CTCA)
- BEACON
  - no reduction of in-hospital duration of stay or hospital admission in the CCTA arm compared with patients investigated with hs-cTn
- ROMICAT II
  - similar results
- RAPID-CTCA
  - CTCA did not improve clinical outcomes at 1 year and was associated with a modest increase in the duration and cost of the hospital stay

RAPID-CTCA trial

- 1748 participants
- Adults with suspected or a provisional diagnosis of ACS (NSTEMI, UA) and one or more of previous coronary heart disease, raised levels of cardiac troponin, or abnormal ECG
- Randomized to:
  - early CTCA and standard of care VS
  - standard of care only
- Primary endpoint
  - all cause death or subsequent type 1 or 4b MI at one year

Gray AJ, et al. RAPID-CTCA Investigators. BMJ.;374:n2106.

RAPID-CTCA trial

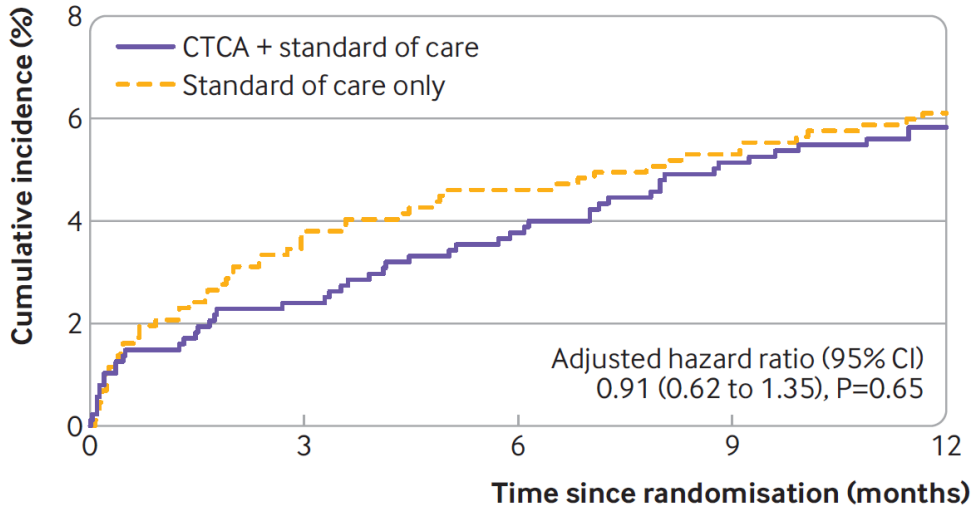


Fig 2 | Cumulative incidence of primary endpoint of one year all cause death or non-fatal myocardial infarction (type 1 or 4b). CTCA=computed tomography coronary angiography

Table 3 | Primary and key secondary outcomes All NS

	CT computed angiography and standard of care (n=877)	Standard of care only (n=871)
Primary outcome		
All cause death or non-fatal myocardial infarction (type 1 or 4b)	51 (5.8)	53 (6.1)
Secondary outcomes		
Death from coronary heart disease or non-fatal myocardial infarction	47 (5.4)	45 (5.2)
Death from cardiovascular disease or non-fatal myocardial infarction	48 (5.5)	46 (5.3)
Non-fatal myocardial infarction	39 (4.4)	40 (4.6)
Death from coronary heart disease	11 (1.3)	6 (0.7)
Death from cardiovascular death	12 (1.4)	8 (0.9)
All cause death	19 (2.2)	17 (2.0)

No significant difference in the primary outcomes between the CTCA and non-CTCA groups (CTCA: 5.8%, non-CTCA: 6.1%, P=0.65) among low-intermediate-risk patients with suspected or provisional ACS

Modest increase in the duration and cost of the hospital stay

- Median hospitalization length of stay was 2.2 days in the CTCA group vs. 2.0 days in the usual care group
- Median costs were also higher by US$718 per patient assessed early on with CTCA

MINOCA ACS

- 8–15% of patients with a clinical diagnosis of MI
- CMR plays an important role in the identification of the causes (plaque rupture/erosion, Takotsubo cardiomyopathy, myocarditis) of MINOCA
- CMR can assess both cardiac structures, function and tissue characteristics
- Patients with a history of acute chest pain followed by a normal stress CMR result have an excellent short- and mid- term prognosis
- In NSTEMI CMR strategy may identify the underlying cause and reduce the need for ICA
- Other non-invasive diagnostic tests such as stress echo, exercise ECG, stress PET/SPECT may be utilised for medically stabilized patients with acute chest pain

2023 ESC Guidelines for the management of acute coronary syndromes

Official ESC Guidelines slide set

ESC
European Society of Cardiology

Recommendations for non-invasive imaging in the initial assessment of patients with suspected acute coronary syndrome

Recommendations	Class	Level
Emergency TTE is recommended in patients with suspected ACS presenting with cardiogenic shock or suspected mechanical complications.	I	C
In patients with suspected ACS, non-elevated (or uncertain) hs-cTn levels, no ECG changes and no recurrence of pain, incorporating CCTA or a non-invasive stress imaging test as part of the initial workup should be considered.	IIa	A
Emergency TTE should be considered at triage in cases of diagnostic uncertainty but this should not result in delays in transfer to the cardiac catheterization laboratory if there is suspicion of an acute coronary artery occlusion.	IIa	C
Routine, early CCTA in patients with suspected ACS is not recommended.	III	B

2023 ESC Guidelines for the management of acute coronary syndromes
(European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad191)

Cons of CTCA as 1st line imaging in CAD

Excluded patients—arrhythmias, tachycardia, severe renal dysfunction, contraindications to beta-blocker—asthma, heart block
Heart rate control—prescription of beta-blocker or rate-limiting calcium channel blocker entailing physician and pharmacy visits before the hospital visit for the CTCA scan
Potential for contrast media reaction
Ionizing radiation exposure
In stable populations referred for CTCA, most individuals do not have obstructive coronary artery disease, leaving the diagnosis and onward management of symptoms uncertain in many referred patients
No data for microvascular function or myocardial ischaemia
Limited specificity for quantifying lumen loss due to atherosclerosis (moderate specificity leading to false positive results), especially within coronary calcification and stents
FFR_{CT} exclusion criteria include history of coronary revascularization, atrial fibrillation
In patients with persisting symptoms and no obstructive CAD, additional visits for downstream functional tests may be necessary, extending the care pathway
In ACS, a CTCA-first strategy has no prognostic benefit, prolongs hospital stay, increases hospital costs
Clinical service: the CTCA scan and report are usually not provided during the initial clinic visit, hence repeated visits are needed
FFR_{CT} adds to initial costs; downstream and overall costs may not increase
Cost-effectiveness uncertain, e.g. SCOT-HEART health economics analysis not available

Take home message

- CTCA should remain targeted for patients assessed to have lower likelihood of CAD due to significant limitations in patients with higher pre-test probability or established coronary heart disease.
- Clinical judgement to choose between CTCA, non-invasive functional testing, and ICA should be exercised in a personalized way

Ευχαριστώ για την προσοχή σας!