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Early invasive versus non-invasive assessment in patients with suspected non-ST elevation acute coronary syndrome

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ABSTRACT

Non-ST elevation acute coronary syndrome (NSTE-ACS) comprises a broad spectrum of disease ranging from unstable angina through to myocardial infarction (MI). International guidelines recommend a routine invasive strategy for managing NSTE-ACS patients at high to very high risk, supported by evidence of improved composite ischaemic outcomes as compared to a selective invasive strategy. However, accurate diagnosis of NSTE-ACS in the acute setting is challenging due to the spectrum of non-coronary disease that can manifest with similar symptoms. Heterogeneous clinical presentations and limited uptake of risk prediction tools can confound physician decision-making regarding the use and timing of invasive coronary angiography (ICA). Large proportions of patients with suspected NSTE-ACS do not require revascularisation but may unnecessarily undergo ICA with its attendant risks and associated costs. Advances in coronary computed tomography angiography and cardiac magnetic resonance imaging have prompted evaluation of whether non-invasive strategies may improve patient selection, or whether tailored approaches are better suited to specific subgroups. Future directions include: 1) better understanding of risk-stratification as a guide to investigation and therapy in suspected NSTE-ACS, 2) randomised clinical trials of non-invasive imaging versus standard of care approaches prior to ICA, and 3) defining the optimal timing of very early ICA in very high-risk NSTE-ACS.

INTRODUCTION

Chest pain remains the most common presenting complaint to hospitals, accounting for 6% of all adult emergency department attendances.[1] However, less than 10% of these visits are due to acute coronary syndrome (ACS).[2] Triage processes that include risk stratification scoring and application of highly sensitive biomarkers have been utilised to better identify patients that can be safely discharged versus those who require inpatient assessment. The application of high-sensitivity troponin (hs-Tn) rapid "rule-in" and "rule-out" algorithms, alongside their recommendation in recent practice guidelines, has substantially reduced time to diagnosis and increased confidence in excluding acute Type 1 myocardial infarction (MI).[3] However, use of such pathways does not reduce subsequent clinical events or facilitate more appropriate selection for ICA.[4] The blurring of boundaries between what constitutes MI and myocardial injury, alongside often normal or non-specific electrocardiogram (ECG) findings,[5] can confound clinical decision-making in patients with suspected NSTE-ACS. The established norm of admitting patients with chest pain and elevated cardiac troponin for further assessment and consideration of ICA largely remains, despite a routine invasive strategy failing to demonstrate a reduction in all-cause mortality or MI in patients with proven NSTE-ACS.[6] Approaches to guide more judicious use of ICA are therefore required. This review will address the contemporary evidence concerning the use and timing of invasive and non-invasive assessment in suspected NSTE-ACS patients. We will focus on the "rule in" cohort that represents approximately 15% of this population, whilst initial hs-Tn testing will "rule out" 55% and lead to further "observation" in 30% of patients.[7] Given the positive predictive value for MI of 70-75% in the "rule in" group,[8] we will review recent studies that have attempted to better identify those patients with Type 1 MI through use of non-invasive imaging modalities. A detailed discussion of Type 2 MI, its differential diagnoses, and subsequent management is beyond the scope of this review.

CURRENT RECOMMENDATIONS AND CONCEPTS

NSTE-ACS patients are a heterogeneous group with a spectrum of disease extending from structurally normal coronary vessels to non-obstructive atherosclerosis and severe occlusive coronary artery disease (CAD). International guidelines recommend a routine invasive strategy in high and very high risk NSTE-ACS based on the clinical scenario and "rule-in" values of hs-Tn,[3 9] with maximal benefit from revascularisation evident in those patients who have the highest baseline risk for future major adverse cardiovascular events (MACE).[10] However, there exists a risk-treatment paradox in NSTE-ACS whereby higher-risk patients are less likely to receive aggressive pharmacotherapy and an early invasive strategy.[11] In addition, current clinical decision pathways result in up to 40% of patients undergoing ICA with no anatomical target for revascularisation,[12] thus suggesting that the risk-benefit ratio of the procedure may be unfavourable in many. Consequently, non-invasive "gatekeeper" imaging strategies prior to ICA have become a focus of contemporary clinical research.

International guidance on the timing of an invasive strategy in NSTE-ACS is displayed in **Table 1**. The 2020 European Society of Cardiology (ESC) NSTE-ACS guidelines, mirrored by the AHA/ACC guidelines (updated in 2014) provide a Class 1A recommendation for an early invasive strategy within 24 hours of hospital admission in high-risk NSTE-ACS.[3 9] However, in a Myocardial Ischaemia National Audit Project (MINAP) database analysis of 137,000 patients discharged with a diagnosis of NSTE-ACS following ICA between 2010 and 2015, only 16% of the high risk group (the high risk group comprised 94% of the total cohort) received an invasive strategy within the ESC guideline recommended timeframe..[13] Conversely, the 2020 National Institute of Health and Care Excellence (NICE) ACS guidelines recommend that a routine invasive strategy is undertaken within 72 hours for patients with an intermediate or higher-risk of MACE according to the Global Registry of Acute Coronary Events (GRACE) score (predicted 6-month mortality >3.0%).[14] Yet despite its strong discriminatory performance for predicting death (c-statistic 0.81) or death combined with non-fatal MI (c-statistic 0.73) at 6 months following discharge,[15] this risk-stratification score is not commonly used in clinical

practice,[16] perhaps due to the misconception that clinical assessment or use of individual risk factors to stratify baseline risk is sufficient.

ICA plays a key role in the diagnosis of atherosclerotic plaque rupture and guides revascularisation with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) in NSTE-ACS. Epidemiological trends indicate an increase in the incidence of NSTE-ACS and rates of ICA in the UK,[17] in part due to the increased detection of myocardial injury by hs-Tn.[4] This presents significant challenges for allocation of limited healthcare resources, including the appropriate use of an early invasive strategy. In the UK, ICA within 24 hours of hospital admission was achieved in 19% of all-comer NSTE-ACS cases during 2018/19, and only 57% within the NICE recommended 72 hours.[18] Moreover, some patients still have to wait for inter-hospital transfer to a facility with on-site coronary revascularisation capability, delaying time to angiography by approximately 24 hours and prolonging inpatient stay.[18] Upstream use of potent anti-thrombotic drugs is recognised to increase bleeding events in those patients awaiting ICA,[19] while in genuine NSTE-ACS cases with threatened coronary occlusion, timely ICA and revascularisation is impeded and increases the risk of recurrent ischaemia and/or abrupt culprit vessel closure. Corroborating evidence comes from a meta-analysis of more than 40,000 patients with NSTE-ACS (mean time to angiography of 31 hours) which found that 25% had a total occlusion of the culprit artery identified at the time of ICA, although this analysis was limited by the precise determination of the timing of coronary occlusion.[20]

There is a pressing need for alternative strategies to improve the targeting of ICA and stratification for revascularisation. Indiscriminate implementation of the ESC guideline recommendations will necessitate significant and costly restructuring of current NSTE-ACS system pathways, potentially to the detriment of other patient groups. To assess the effect of GRACE score risk stratification in ACS pathways (STEMI and NSTE-ACS), the Australian GRACE Risk Intervention Study found an increased utilisation of early ICA with a GRACE stratified approach, however this did not change the final

treatment plan or reduce cardiovascular outcomes at 6 months.[21] An alternative pragmatic strategy is to use non-invasive imaging to triage and select patients who will potentially benefit from ICA. The ESC guidelines currently recommend coronary computed tomography angiography (CCTA) as an alternative to ICA in suspected NSTE-ACS patients with low-intermediate risk of CAD, and in situations when cardiac troponin and/or ECG findings are normal or inconclusive (**Table 1**).[3] However, this guidance is only applicable to a small minority (approximately 6%) of NSTE-ACS patients admitted for inpatient assessment in the UK.[13] Its broader role as a gatekeeper strategy in suspected NSTE-ACS is yet to be clearly defined.

AN EARLY INVASIVE STRATEGY

A series of randomised trials have investigated the optimal timing of ICA and whether early (<24 hours from admission) angiography revascularisation results in improved clinical outcomes as compared to delayed or standard of care approaches (typically within 72 hours).[22-35] Significant variations in study design, inclusion criteria, timing of ICA, and endpoint definitions have resulted in conflicting and disparate results that are challenging to interpret and apply to current practice (**Figure 1**). When these data are evaluated in totality through patient-level data meta-analysis, no differences in hard clinical endpoints between an early versus delayed invasive strategy have been demonstrated in unselected NSTE-ACS, yet a signal of benefit from expeditious revascularisation in high-risk GRACE score >140 patients was observed.[36] Two large randomised trials (TIMACS[26] and VERDICT[32]) with important *a priori* high-risk subgroup analyses (**Figure 2**) primarily inform the recently updated ESC NSTE-ACS guidelines.[3]

The TIMACS trial randomly allocated 3031 unselected patients with NSTE-ACS to either an early (median 14.0 hours) or delayed strategy.[26] Despite no overall difference in the 6-month primary outcome of death, MI or stroke, in 961 high-risk GRACE score >140 patients an early invasive strategy reduced the risk of the primary endpoint by 35.0%. Similarly, the VERDICT trial randomised 2147 NSTE-

ACS all-comers to standard of care invasive or accelerated early invasive (median 4.7 hours) strategies and demonstrated no difference in the primary composite endpoint (death, MI, refractory ischaemia, and admission for heart failure) at 4.3 years, but improved outcomes in GRACE score >140 patients.[32] Furthermore, the recent EARLY trial tested an immediate versus delayed invasive strategy in 709 NSTE-ACS patients, of which 93% were high-risk according to ESC criteria (median GRACE score 122).[34] The primary composite endpoint (cardiovascular death and recurrent ischaemic events) was significantly lower in the very early arm (4.4% vs. 21.3%, $p<0.001$), driven by a reduction in recurrent ischaemic events. This study was limited by short follow up and a lack of upfront antiplatelet loading prior to angiography which may account for the increased ischaemic events observed in the control arm. It remains to be seen whether hard clinical outcomes will differ in the longer term. The available data suggest that the benefit of an early invasive strategy may be strongly associated with a patient's baseline risk profile. However, the subgroup analyses from TIMACS and VERDICT should be interpreted with caution and considered as hypothesis generating. Both studies utilised conventional troponin or CK-MB for the diagnosis of NSTE-ACS, and hence, the conclusions may not be directly translatable to the current hs-Tn era.

As such, the current ESC guideline mandating that an invasive strategy should be undertaken within 24 hours in high-risk patients (Class 1A) is open to scrutiny. Data that support early ICA in high-risk patients are from the two aforementioned subgroup analyses and solely established on GRACE score >140 thresholds, and not using the dynamic change at lower levels of hs-Tn that predominates in the ESC high-risk criteria.[3] Although the interpretation from a condensed meta-analysis is that an early invasive strategy may reduce mortality in higher-risk patients (including those with elevated biomarkers),[36] major restructuring and expansion of ACS pathways requires prospective data that specifically investigates robustly defined higher-risk NSTE-ACS patients. This important and pertinent clinical question therefore remains unanswered and should be an area of focus in future randomised pragmatic strategy trials appropriately powered for hard clinical endpoints.

A NON-INVASIVE STRATEGY

Studies from the era of early generation troponin assays have tested upfront non-invasive imaging to rule out MI in low-risk patients with suspected NSTE-ACS,[37] [38] although the excellent negative predictive value (NPV) of rapid hs-Tn assays have now rendered this strategy largely redundant.[39] The high sensitivity of newer generation troponin assays has come at the at the expense of specificity, prompting the investigation of alternative strategies to augment diagnostic yield in suspected NSTE-ACS. Recent advances in non-invasive imaging have raised the prospect of an expanded role in the early triage of suspected NSTE-ACS patients and improved targeting of ICA. CCTA provides accurate anatomical visualisation of the coronary lumen and arterial wall making it well suited for the non-invasive assessment of atherosclerotic plaque rupture events (**Figure 3**). The application of CCTA to support decision-making in suspected NSTE-ACS is a field of active clinical research and several clinical trials have recently reported on its potential to serve as a 'gatekeeper' to the catheter laboratory. Alternative non-invasive imaging modalities include multiparametric stress perfusion cardiac magnetic resonance (CMR) which can phenotype the myocardium and provide unique insights into the pathophysiology of MI and myocardial injury (**Figure 4**). Recent studies support the role of CMR in clarifying the aetiology of biomarker elevation in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA),[40] and identifying the culprit artery when compared with ICA in suspected NSTE-ACS patients.[41]

Recent ESC guidelines recommend that both modalities are used solely in low-risk patients (normal or inconclusive ECG/troponin) to guide a downstream invasive strategy.[3] Upfront non-invasive imaging strategies using CCTA and CMR approaches have been reported in recent trials specifically addressing the safety, accuracy and efficacy of these techniques compared to with standard of care in suspected NSTE-ACS populations.

Non-invasive assessment strategy trials in suspected NSTE-ACS

The BEACON study was the first of such investigations in the hs-Tn era. Randomising 500 patients with acute chest pain (without known CAD) to either upfront CCTA or standard of care diagnostic work-up strategies, the primary endpoint of identification of CAD requiring revascularisation within 30 days was no different (8.8% vs. 6.8%, p=0.40).[42] However, the CCTA approach was safe and associated with less outpatient testing and reduced costs. The major limitation of the study was that only 10% of the population had an hs-Tn greater than the 99th centile, thus the need for further downstream investigations in many was obviated.

In a pre-planned pragmatic observational substudy of the aforementioned VERDICT trial, upfront blinded CCTA prior to ICA was tested in both early and standard care ICA groups. Selecting a primary endpoint of CCTA to exclude ≥50% coronary artery stenosis, in approximately 1,000 patients CCTA was found to have a high diagnostic accuracy to rule in (88% positive predictive value) and rule out (91% NPV) obstructive CAD when ICA was used as the reference standard.[43] This finding was not influenced by patient characteristics or risk profile and no significant differences between the study arms were observed. Reassuringly, the majority of the 2.3% of patients with a false negative CCTA had small side-branch disease of lower prognostic significance, while the rate of non-diagnostic CCTA was a modest 5.2%. The somewhat arbitrary and debatable endpoint of coronary stenosis threshold ≥50% (and its relevance to those lesions that subsequently undergo revascularisation) is questionable, whilst exclusion criteria of atrial fibrillation, previous CABG, and impaired renal function should be noted. However, the overarching message is that a strategy of upfront CCTA as a triage to ICA in NSTE-ACS is feasible, but requires testing in a large, randomised clinical outcomes trial. Moreover, the role of CCTA in longer-term risk stratification of NSTE-ACS may also be of value, since a further analysis of VERDICT demonstrated prognostic equivalence as compared to ICA in predicting outcomes of patients with obstructive and high-risk patterns of CAD.[44]

The three-arm, prospective randomised controlled CARMENTA trial compared upfront CCTA or CMR with routine ICA in patients with suspected NSTE-ACS and inconclusive ECG findings.[45] Following randomised allocation of 207 patients, clinicians received the results of upfront imaging tests prior to decision-making regarding ICA, with the expectation that ICA would be avoided if findings were reassuring. Compared to routine care, the primary efficacy endpoint of referral to ICA was reduced by one-third in the CCTA arm ($p<0.001$ vs. routine), while CMR reduced this by 13% ($p<0.001$ vs. routine). Of significant interest was physician behaviour following the initial strategy. Clinician confidence in a negative CCTA was borne out by greater reduction in referral to ICA, likely due to the fact CCTA is an anatomical modality. Furthermore, in the non-CMR arms 67% of patients (33/49) underwent CMR when there was diagnostic uncertainty of NSTE-ACS, with a clinically relevant diagnosis made in nearly 50% (16/33), underlining the valuable role of CMR in accurate characterisation of myocardial structure and function. In a further subanalysis, diagnostic accuracy of CMR was reported to be 77% in detecting obstructive CAD using T2-weighted and late gadolinium enhancement imaging in the setting of suspected NSTE-ACS.[46]

More recently, the RAPID CTCA trial evaluated whether early CCTA improved clinical outcomes among intermediate to high-risk patients with suspected NSTE-ACS.[47] Enrolling 1,748 symptomatic patients with at least one of: prior CAD , elevated hs-Tn and abnormal ECG, the primary outcome of all-cause mortality, Type 1 or Type 4b MI (stent thrombosis) was reported to be no different between the two strategies. While the final manuscript is yet to be published, RAPID CTCA indicates that there is likely no need for upstream CCTA in NSTE-ACS patients at higher-risk.

Implications of contemporary data and future directions

There is a clear clinical and economical need for refined diagnostic pathways in suspected NSTE-ACS. Unnecessary downstream testing, including ICA, may be attenuated by recent advances in the applicability and feasibility of non-invasive imaging modalities to assess for the presence of

obstructive CAD (**Table 2**). Rather than a 'one test for all' approach for patients with suspected NSTE-ACS, we would argue that a testing strategy should be guided by a clinician's certainty of suspected NSTE-ACS so that the 'right patient gets the right test at the right time'. In patients with a high clinical gestalt of NSTE-ACS, delaying ICA to perform non-invasive imaging would appear to be counter-intuitive. However, biomarker evidence of myocardial injury in those patients with more ambiguous presentations may benefit from early anatomical evaluation with CCTA to exclude significant CAD and thus preclude subsequent ICA (**Figure 5**). Challenges lie in overall service provision of this approach given the acknowledged lack of cardiac CT capacity within the UK,[48] as up to approximately 25% of patients with suspected NSTE-ACS would be eligible for our proposed strategy based on mild elevation of hs-Tn.[49] The role of CMR in this paradigm is less clear, but its strength in providing diagnostic clarification requires further investigation.

Ongoing clinical research is required to better define future diagnostic strategies in this heterogeneous and challenging population. Further issues that require investigation:

- Does application of robust risk-stratification criteria (i.e., GRACE score) increase guideline-indicated treatment and improve clinical outcomes in NSTE-ACS? This will be answered by the UKGRIS study.[50]
- Can routine non-invasive imaging approaches prior to ICA, powered for clinical endpoints, demonstrate clinical effectiveness and cost-efficacy when compared to standard of care approaches?
- Do high-risk NSTE-ACS patients (defined by robust risk stratification criteria) benefit from very early ICA and follow-on revascularisation?

Conclusion

In NSTE-ACS, benefit from early ICA and revascularisation is closely associated with baseline risk, yet the optimal means of selecting patients who will profit from this approach remains unclear. Early non-

invasive imaging assessment with CCTA or CMR may help identify lower-risk populations who can safely avoid unnecessary ICA, but further large, randomised trials are required to prove clinical and cost effectiveness.

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Table 1: International guidelines for the timing of an invasive strategy in patients with NSTE-ACS			
	Very high-risk	**High-risk**	**Low risk**
European Society of Cardiology, 2020[3]	An immediate invasive strategy (**<2h**) is recommended in patients with at least one of the following criteria: ▪ Haemodynamic instability or CGS ▪ Recurrent or refractory chest pain ▪ Life-threatening arrhythmia ▪ Mechanical complications of MI ▪ Heart failure clearly related to NSTE-ACS ▪ Presence of ST-segment depression >1mm in >6 leads additional to ST-segment elevation in aVR and/or V1	An early invasive strategy (**<24h**) is recommended in patients with any of the following high-risk criteria: ▪ Diagnosis of N-STEMI as per accepted definition ▪ Dynamic or presumably new contiguous ST-T-segment changes suggesting ongoing ischaemia ▪ Transient ST-segment elevation ▪ GRACE risk score >140	A selective invasive strategy after appropriate ischaemia testing or detection of obstructive CAD by CTCA is recommended in patients considered at low risk
American Heart Association/American College of Cardiology, 2014[9]	An urgent/immediate invasive strategy is indicated in patients with NSTE-ACS who have: ▪ Refractory angina ▪ Haemodynamic or electrical instability	An early invasive strategy (**<24h**) is indicated in initially stabilised patients with NSTE-ACS who have an elevated risk for clinical events: ▪ GRACE score >140 ▪ Temporal change in troponin ▪ New or presumably new ST depression	For those not at high/intermediate risk, a delayed invasive approach (**25 to 72h**) or ischemia guided strategy is reasonable

Colour coding represents the class of guideline recommendation (green: class I, yellow: class II).
NSTE-ACS: non-ST segment elevation acute coronary syndrome; N-STEMI: non-ST elevation myocardial infarction; CGS: cardiogenic shock; MI; myocardial infarction; GRACE; Global Registry of Acute Coronary Events; CAD; coronary artery disease; CTCA: computed tomography coronary angiography

Table 2: Potential benefits and limitations of invasive versus non-invasive strategies

Early invasive strategy	
Benefits	**Limitations**
Rapid mechanical stabilisation and achievement of culprit vessel patency	Reduced time for pharmacological passivation (i.e., thrombus stabilisation by antiplatelet and antithrombotic agents) and potential for increased risk of thrombotic embolisation resulting in higher rates of Type 4a MI
Lower associated healthcare costs due shorter inpatient hospital stays	Requires major and costly restructure and expansion of current NSTE-ACS pathways in order to fulfil service delivery
Reduced bleeding events during pre-ICA period from upstream use of potent anti-platelet and anti-thrombotic agents	Rapidity of approach allows shorter time period to discriminate between potential causative pathologies – unnecessary and indiscriminate ICA may result
	Prolonged hospitalisation if service capacity cannot meet clinical demand
Early non-invasive strategy	
Benefits	**Limitations**
Reduction in number of patients exposed to risks of invasive investigations (e.g., bleeding, vascular complications)	Requires major and costly restructure and expansion of CTCA/CMR capacity including training of new staff to deliver service
Identification of culprit lesion to guide subsequent PCI	Delays time to revascularisation in those patients that do require PCI (e.g., imminent vessel closure) – although large strategy trials have not demonstrated worse outcomes in all-comer populations
Early identification of non-coronary disease (e.g., PE, aortic dissection)	Prolonged hospitalisation if service capacity cannot meet clinical demand
Potential for health economic savings if expensive invasive procedures are avoided (e.g., particularly inter-hospital transfers from centres without on-site catheter laboratory facilities)	

CTCA: computed tomography cardiac angiography; CMR: cardiac magnetic resonance; ICA: invasive coronary angiography; MI: myocardial infarction; NSTE-ACS: non-ST elevation acute coronary syndrome; PCI: percutaneous coronary intervention; PE; pulmonary embolism

FIGURE LEGENDS

Figure 1: Summary of randomised trials comparing early and delayed invasive strategies in NSTE-ACS

Bars represent interquartile ranges and median times from randomisation to invasive coronary angiography.
*Significant heterogeneity in primary endpoints must be noted (e.g., non-clinical outcomes such as enzymatic infarct size). ISAR-COOL findings driven by reduction in non-fatal MI in early group; OPTIMA findings driven by increase in non-fatal MI in early group, SISCA findings driven by reduction in urgent revascularisation in early group; RIDDLE-NSTEMI findings driven by reduction in non-fatal MI in early group, EARLY findings driven by reduction in recurrent ischaemic events in early group.

This figure has been reproduced with permission and adapted from *Jobs et al, Lancet 2017*[36]

NSTE-ACS: non-ST segment elevation acute coronary syndrome; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Figure 2: Subgroup analysis of high-risk patients (GRACE risk score >140) in TIMACS and VERDICT trials for the primary endpoint

Primary outcome for TIMACS is death, MI or stroke at 6 months; and primary outcome for VERDICT is death, MI, hospitalisation for myocardial ischaemia or heart failure at a median follow-up of 4.3 years.
GRACE: Global Registry of Acute Coronary Events; HR: hazard ratio; MI: myocardial infarction.

Figure 3: Coronary CT Angiography in NSTE-ACS

Non-invasive coronary CT angiography provides high isotropic resolution of the coronary lumen and arterial wall in the evaluation of plaque rupture events. **A** In suspected NSTE-ACS, CCTA demonstrated a low attenuation mixed morphology plaque in the left main stem with plaque rupture and intracoronary thrombus formation (yellow arrow). **B** Multiplanar reconstructions facilitate cross-sectional interrogation of the arterial wall to assess for vulnerable plaque features including positive remodeling and low attenuation cores (***blue inset***) in addition to luminal stenosis severity (***red inset***). **C** This can help support clinical decision-making at the time of invasive coronary angiography.
CCTA: computed tomography coronary angiography; NSTE-ACS: non-ST elevation acute coronary syndrome

Figure 4: Cardiac Magnetic Resonance in NSTE-ACS

A In clinically ambiguous cases, cardiac magnetic resonance imaging can be used to identify regions of acute myocardial oedema to account for myocardial injury (red and green arrows). **B** Late gadolinium enhancement (LGE) and **C** T1 parametric mapping can be used to assess the extent and distribution of myocardial oedema to support culprit plaque treatment at the time of **D** invasive coronary angiography. **E** In complex cases, cardiac magnetic resonance can be used to detail the distribution and transmurality of infarction (yellow arrows) and assess of complications such as thrombus formation (blue arrow). **F** Microvascular obstruction on LGE (red arrow) and **G** oedema/fibrosis on T1 mapping (green arrow) provide incremental information to guide **H** coronary intervention compared with standard of care assessments.

Figure 5: Proposed diagnostic algorithm for suspected NSTE-ACS in the era of high-sensitivity troponin

CGS: cardiogenic shock; CCTA: cardiac computed tomography angiography; CMR: cardiac magnetic resonance; ECG: electrocardiogram; hs-Tn: high-sensitivity troponin; ICA: invasive coronary angiography; MINOCA: myocardial infarction with non-obstructive coronary arteries; NSTE-ACS: non-ST elevation acute coronary syndrome; STEMI: ST elevation myocardial infarction; TTE: transthoracic echocardiography.