**NICE guidelines on myocardial revascularisation**

Commissioned article by *Heart* editorial team

Richard Jabbour1, Nick Curzen1,2

1Coronary Research Group, University Hospital Southampton NHS Foundation Trust, Southampton, SO16 6YD, UK.

2Faculty of Medicine, University of Southampton, Southampton, SO16 6YD, UK.

Conflicts of interest statement:

N. Curzen – unrestricted research grants from: Boston Scientific; Heartflow; Beckman Coulter. Speaker fees/consultancy from: Abbot Vascular; Heartflow; Boston Scientific;

Travel sponsorship – Edwards; Biosensors, Abbot, Lilly/D-S; St Jude Medical, Medtronic.

R. Jabbour – none declared

Contributorship statement:

RJ and NC contributed equally to this manuscript. NC provided expert appraisal and additional viewpoints.

**Corresponding Author:**

Prof Nick Curzen

Wessex Cardiothoracic Centre

University Hospital Southampton NHS Trust

Southampton

SO16 6YD, UK

Nick.curzen@uhs.nhs.uk

**Abstract (up to 250 words)**

Cardiologists in the United Kingdom predominantly use the National Institute for Health and Care Excellence (NICE) and European Society of Cardiology (ESC) guidelines to help guide decision making. This article will appraise the current recommendations from NICE regarding myocardial revascularisation and compare them to other major international guidelines.Whilst there are many similarities, subtle differences exist. These differences arise in part due to the evidence base at time of publication, but also from the different healthcare systems that they are designed for, and from the cost-effectiveness models that dominate the methodology used by NICE. The clinical implications of the differences between the international guidelines will be analysed.

**Introduction**

Cardiologists in the United Kingdom use the NICE and ESC guidelines to help guide decision-making. This article will appraise the current recommendations from NICE regarding myocardial revascularisation, including some aspects of antiplatelet therapy, and compare them to other major international guidelines. Whilst there are many similarities, subtle differences exist. These differences arise in part from the date of publication and therefore evidence base used, but also from the different healthcare systems that they represent, and from the cost-effectiveness models that dominate the methodology used by NICE. There is no single NICE guideline concerning myocardial revascularisation, but recommendations are made within NICE guidelines about stable angina and acute coronary syndromes.1,2 The evidence base regarding the prognostic and symptomatic benefit of myocardial revascularisation is different for chronic and acute coronary syndromes, so these will be analysed separately.3–6

**Stable coronary artery disease / chronic coronary syndrome (CCS)**

*Diagnosis*

The recommendations from NICE regarding diagnosis are summarised in Figure 1 and compared to other guidelines in Table 1. NICE was an early adopter of CT coronary angiography (CTCA), which is the first line investigation in the “Chest pain of recent onset” NICE CG95 guidelines if clinical assessment indicates typical or atypical angina, or if there are pathological ST segment or T-wave changes or Q waves on the resting ECG.7 In other words, these guidelines recommend CTCA as the frontline test for the majority of patients. Furthermore, the NICE Technology Appraisal of FFRCT (MTG32) recommends this complementary test as an alternative option for patient with stable, recent-onset chest pain.8 Whilst the use of CTCA is expected to reduce the number of patients requiring diagnostic invasive coronary angiography(ICA), it does not theoretically influence the proportion being offered revascularisation as it does not assess ischaemia. By contrast, liberal use of FFRCT has the potential to reduce the rate of ICA significantly, as has been demonstrated in PLATFORM and FORECAST.9,10

*Indications for revascularisation*

The importance of optimal medical therapy is stressed in the NICE guidelines (Stable angina: management; CG126). Specifically: 1) an angiogram is predominantly recommended for patients whose symptoms are not satisfactorily controlled on optimal medical therapy(OMT)2, and 2) revascularization(PCI or CABG) considered in patients who have refractory symptoms despite OMT.2 However, in the subset of patients who are controlled on medical therapy, CABG can be considered to improve prognosis in a subgroup of people with left main stem or proximal three-vessel disease.2 By contrast, there is no mention of prognostic benefit for PCI.

The ESC myocardial revascularisation guidelines provide didactic recommendations for revascularisation in CCS including: 1) left main with 50% stenosis(class IA); 2) proximal LAD >50%(class IA); 3) 2 or 3 vessel with >50% stenosis with LVEF≤35%(class IA); 4) large area of ischaemia(>10%) or abnormal FFR(class IA) or 5) single remaining coronary artery with stenosis > 50%(class IC).6 Numbers 1), 2), 3), & 5) of these ESC indications for revascularisation must in addition have documented ischaemia or be a haemodynamically relevant lesion (FFR <0.80 or iwFR <0.89). A lesion without ischaemia must be >90% on angiographic appearance to qualify for revascularisation. Revascularisation to improve symptoms is addressed separately and is recommended for haemodynamically significant coronary lesions in the presence of limiting angina, or angina equivalent, with insufficient response to optimised medical therapy(class IA).2,11

Recently, the UK REVIVED-BCIS2 trial, which evaluated the efficacy of PCI compared to OMT for patients with ischaemic EF<35% has been reported. Over a median follow-up of 41months, event rates were high (37.2% PCI group vs 38.0% OMT; p=0.96) but not different between groups and, notably, the change in left ventricular ejection fraction was also not significant. Future guidelines will likely incorporate these findings into their recommendations.12

*PCI versus CABG*

NICE guidelines stress the importance of regular Heart Team meetings to discuss the risks and benefits of drug treatment alone and/or define the revascularisation strategy.2 In symptomatic patients in whom either CABG or PCI might be appropriate, NICE recommends that the risks and benefits of PCI and CABG are explained to the patient and, if no preference is expressed, the evidence which suggests that PCI may be the more cost-effective procedure should be considered when deciding. 2 As with all such guidelines, some of the most recent data(in this case comparing PCI and CABG)3,4 are not included and regarding cost-effectiveness indicate that CABG may have relative cost benefits over PCI.13

Regarding multivessel disease, it is recommended that the potential survival benefit of CABG should be taken into account in patients with diabetes, age>65, and anatomical three vessel disease (3VD) with or without involvement of left main stem.2 CABG is also preferred for left main/proximal 3VD.2 In contrast to NICE, PCI or CABG is recommended in the ESC guidelines for one-vessel CAD with proximal LAD stenosis(class IA).6 CABG is also recommended to improve survival(class 1B) in stable patients with multivessel CAD and severe ischaemic left ventricular systolic dysfunction(LVEF≤35%).6

*Use of SYNTAX score*

No specific complexity tool is recommended by NICE, but it is clearly stated that anatomical complexity should be taken into account when considering the best mode of revascularisation.2 By contrast, the SYNTAX score is recommended by ESC for use in left main and/or 3VD(class 1B).6 For example, ESC guidelines state that CABG is 1st line for patients with significant left main stem disease with SYNTAX score >33(class IA) and for patients with 3VD either with intermediate/high SYNTAX score(≥23; class IA), or if diabetic, irrespective of SYNTAX score(class IA).6 On the other hand, PCI is recommended as an option for patients with left main stem disease with low SYNTAX score(≤22; class IA) and 3VD without diabetes mellitus and low SYNTAX score(class IA).6

*Comparison with ACC/AHA/SCAI guidelines*

The most recently published revascularisation guidelines are those from ACC/AHA/SCAI. These are generally more in line with NICE and, specifically, are more conservative than the ESC regarding revascularisation in CCS.5 As such, these guidelines have proved relatively contentious. For example, in stable multivessel disease, CABG/PCI has a class IIb(“may be considered”) recommendation.5 Proximal LAD disease with normal LV function also has a lower, class IIb recommendation, citing uncertain benefit.5 The SYNTAX score also has a downgraded recommendation(class IIb) for use in 3VD. Finally, regarding left main disease there is also a lower recommendation for PCI(class IIa) in selected stable patients with low to medium anatomical complexity for whom PCI can provide equivalent revascularisation to CABG. 5

**Acute Coronary Syndrome**

**STEMI**

The evidence for revascularisation in STEMI is well established from multiple randomised controlled clinical trials and is reflected in the similarities between the major guidelines. The recommendations from NICE regarding STEMI are summarised in Figure 2 and compared to other guidelines in Table 2.

*Indications for PCI*

NICE guidelines state that PCI should be offered if presenting within 12 hours of symptom onset and PCI can be delivered within 120 mins of diagnosis.1 Coronary angiography, with follow-on primary PCI if indicated, should be considered for people with acute STEMI presenting more than 12 hours after the onset of symptoms if there is evidence of ongoing myocardial ischaemia or cardiogenic shock.1 Fibrinolysis should be offered to patients presenting within12 hours of symptom onset if PCI cannot be delivered within 120 mins. If there is evidence of residual ST elevation 60-90 minutes after administration, rescue PCI should be offered immediately. Coronary angiography should be considered in all stable patients post fibrinolysis during the index hospital admission. 1

The ESC and ACC/AHA/SCAI guidelines are generally concordant regarding timing and suitability of PCI, but have slightly longer timeframes.5,6 For example, in the ESC guidelines, PCI is recommended for patients who present <12 hours, but it is also considered reasonable for STEMI patients within 12-48 hours(class IIa).6 In the ACC/AHA/SCAI guidelines, PCI has a similar class I indication for <12hours, but a longer time window of 12-24hours is given a class IIa recommendation.5

In both guidelines, PCI(or surgery if PCI not feasible) is recommended in patients with cardiogenic shock or hemodynamic instability irrespective of symptom onset. Rescue PCI has a class I indication after failed fibrinolysis in the ESC guidelines.5,6

In the ESC guidelines, fibrinolysis recommendations are similar to NICE.6 In the updated American guidelines, no specific details are given regarding timing of fibrinolysis in STEMI, but rescue PCI is recommended(class I) after failed lytic therapy. Importantly, routine invasive angiography is recommended 3-24hours after any fibrinolysis therapy is given(class IIa).5

*Complete Revascularisation*

NICE recommends revascularisation of non-culprit arteries following primary PCI in patients who have significant bystander disease. Furthermore, complete revascularisation should be performed during the index hospital admission.1 By contrast, only the culprit vessel should be treated during the index procedure for STEMI patients with cardiogenic shock.1

The ESC and ACC/AHA/SCAI guidelines regarding complete revascularisation in STEMI are concordant with NICE. For example, ESC guidelines specify a class IIa recommendation for non-IRA lesions before hospital discharge.6 In the ACC/AHA/SCAI guidelines, staged percutaneous intervention(in hospital or after discharge) of bystander disease is recommended(class I) if the vessel supplies a large area of myocardium and the patient has few comorbidities.5 In addition, PCI of non-culprit vessel(s) at the time of primary PCI may be considered(class IIb) in stable patients with uncomplicated revascularization of the culprit artery, low complexity non-culprit artery disease, and normal renal function.5 Regarding STEMI and cardiogenic shock, the NICE, ESC and ACC/AHA/SCAI guidelines are concordant in recommending that PCI of non-infarct arteries should not be performed at the time of primary PCI because of the higher risk of death or renal failure(class III).1,5,6

*Antiplatelet therapy*

NICE recommends that aspirin 300mg should be administered immediately after diagnosis, and that a P2Y12 inhibitor be given early before primary PCI. NICE recommends that prasugrel is used as the first line P2Y12 inhibitor in patients who are not taking an oral anticoagulant. Clopidogrel is recommended in patients who are taking an oral anticoagulant.1 In contrast to NICE, ESC and ACC/AHA/SCAI guidelines offer no preference for either prasugrel or ticagrelor. 5,6

*Access route and anticoagulation*

NICE recommends radial, rather than femoral arterial access should be considered for STEMI patients undergoing emergency coronary angiography. Unfractionated heparin is recommended as the peri-procedural anticoagulant of choice in transradial cases, with use of bailout glycoprotein IIb/IIIa, if required. Consideration should be given to using bivalirudin with bailout GPI if femoral access is used.1 Routine use of thrombus aspiration during primary PCI is not recommended. These recommendations are generally consistent with ESC and ACC/AHA/SCAI guidelines.5,6

**NSTEMI**

*Risk stratification*

NICE guidelines regarding unstable angina/NSTEMI recommend the use of the Global Registry of Acute Coronary Events(GRACE) scoring system to guide treatment.1 In patients with a predicted 6-month mortality >3%, angiography should be considered within 72 hours, presuming no contraindications exist. By contrast, in patients with a predicted 6-month mortality ≤3%, conservative management should be considered. Regardless of predicted risk, patients with clinical features indicating instability are recommended to undergo urgent angiography.1 The recommendations from NICE regarding NSTEMI are summarised in Figure 3 and compared to other guidelines in Table 3.

In the ESC guidelines, the approach is rather different regarding both use of risk scores and timing of angiography. Whilst GRACE risk score models are recommended for estimating prognosis(class IIa), the decision to perform angiography is generally based on the presence or absence of “very high” risk(haemodynamic instability, refractory chest pain, life threatening arrhythmia, mechanical complications, acute heart failure related to ACS, ST elevation in aVR with broad ST depression>1mm) or “high” risk criteria(NSTEMI diagnosis, dynamic ST/T changes, resuscitated cardiac arrest without ST segment elevation, GRACE score >140).6 If very high-risk criteria are present an immediate invasive strategy(<2 hours) is recommended(class I), whilst an early invasive(<24hours) is recommended for high-risk criteria(class I). If low risk(lack of very high / high risk characteristics) then a selective invasive strategy can be followed(class I) after appropriate ischaemia testing or CTCA. 6

In the ACC/AHA/SCAI guidelines, an invasive strategy is recommended(class 1) for patients at elevated risk of recurrent ischaemic events are appropriate candidates for revascularisation.5 Similarly, to NICE/ESC, emergency revascularisation is recommended for patients in cardiogenic shock, those with refractory angina, or hemodynamic or electrical instability(class I).5 However, in contrast to NICE, an earlier invasive strategy(<24 hours) is considered a reasonable approach(class 2a) in stabilized patients at high risk for ischemic events.5 Furthermore, in these guidelines, it is also considered reasonable to revascularise before hospital discharge if determined to be at an intermediate or low risk of clinical events(class 2a).5

*Antiplatelet therapy*

In the NSTEMI population, NICE recommends ticagrelor with aspirin as first choice DAPT regime unless a patient has high bleeding risk, in which case clopidogrel with aspirin is advised.1 In contrast, in the ESC guidelines prasugrel is recommended for patients who proceed to PCI(class IIa). 6 In the ACC/AHA/SCAI guidelines, no preference is given to ticagrelor or prasugrel but both are preferred to clopidogrel(class IIa).5

**Discussion**

**Prognostic evidence to support revascularisation over medical therapy in stable patients**

*Left Main Disease*

The evidence for prognostic benefit from CABG over medical therapy in patients with left main stem disease is predominantly from historical randomised trials which predated the use of disease-modifying drugs, most notably statins. Contemporary trials comparing revascularisation with medical therapy have excluded patients with left main stem disease.14–19 There is no randomised trial evidence that PCI offers prognostic advantage over OMT in left main disease; for example, left main disease was an exclusion to randomisation in ISCHEMIA.3 However, there are both randomised and observational data to suggest equivalent mortality after PCI and CABG in left main patients who are suitable for both. Perhaps therefore, we can infer that PCI also has prognostic advantage in patients with left main disease. A meta-analysis of 19 historical left main studies found equivalent mortality rates between CABG and PCI, and that both were associated with superior survival compared with medical therapy.20 This is also consistent with another recent meta-analysis which reported no difference in all-cause death at 5 years overall; although, by using Bayesian analyses, a slight increase in cumulative risk of death with PCI of 1% (0.2% per year) was found.21 In addition, a recent meta-analysis of contemporary trials also found similar major adverse cardiovascular events between PCI and CABG, although repeat revascularisation procedures were significantly higher for PCI.22 However, It seems highly unlikely that there will ever be a randomised trial comparing PCI versus OMT alone in patients with significant LM disease. Whilst randomised data are rightly considered to carry the most scientific validity, the findings of large-scale observational studies have complementary value, given that they include a much larger representation of the real-world population of patients that we look after in routine practice. The observational long-term data for patients with 3VD, when comparing multivessel PCI with CABG, are consistent with the 10-year results in SYNTAXES, thus adding weight to the concept that there is indeed a difference in long term mortality. 23,24

*Three Vessel Disease*

In this sub-group, the historical evidence does suggest survival advantage for CABG over medical treatment, although these data again largely pre-date the advent of disease-modifying medical therapy.14,19 When comparing CABG versus PCI, a recent meta-analysis reported a mortality benefit of CABG in diabetics with multivessel disease and higher coronary complexity.25 However, recent data from ISCHEMIA is concordant with the results of prior RCTs which did not show a survival advantage for PCI or CABG over medical therapy, allowing for the exclusion of left main disease.3 It must be noted that, regarding proximal LAD disease, whilst an early meta-analysis showed a benefit with CABG over medical therapy, the dedicated MASS trial did not.26 It is notable that in the ISCHEMIA trial, 46.8% of patients had significant proximal LAD disease and *post hoc* analysis demonstrated no heterogeneity of treatment effect for the primary outcome.3, 19,26–30 A more recent, relevant, observation which has not yet influenced the guidelines are the 10-year survival of the patients in the SYNTAX trial.24 In this SYNTAXES study, survival at 10 years was significantly better in the CABG group compared with PCI in those with 3VD, but no difference was seen in LM patients.

*SYNTAX*

One of our highlighted areas of disparity between NICE and ESC is the recommended use of anatomical scoring systems to guide decision making. For example, in the ESC guidelines, there is a stronger recommendation to use SYNTAX score to decide between PCI or CABG in patients with left main or 3VD. Although the 5 year data of the SYNTAX trial were not available at the time of NICE publication, this was taken into account in the 2016 reappraisal and, even so, no update to the original 2011 guidance was made.24,31 The more recent ACC/AHA/SCAI guidelines have a lower level of recommendation for the use of SYNTAX, which is more in line with NICE, and is due mainly to poor interobserver variability and lack of clinical variables included in the score that are known to affect periprocedural outcome.5 The guidelines may evolve with the development of more sophisticated scoring tools that take account of anatomy and key clinical variables.

*NSTEMI*

There is a discrepancy between the speed with which patients are put forward for coronary angiography when they present with high risk NSTEMI. In fact, despite the availability of numerous randomised trials, the evidence base for an early invasive strategy(< 24 h) in patients with NSTE-ACS is relatively sparse. The VERDICT and TIMACS trials did, however, demonstrate benefit from the early strategy in the subgroups of patients with GRACE risk score >140, but, of course, this must be examined with caution, given that it represents an unpowered secondary analysis.32,33 In reality risk scores such as GRACE are rarely used in the UK which may also complicate interpretation.34 A recent meta-analysis suggests no clinical outcome advantage for very early angiography, but shorter hospital stay.35

*STEMI*

There are now 7 randomised trials reporting clinical outcome benefit from primary PCI to the infarct-related vessel and complete PCI revascularisation of bystander disease in STEMI patients. 36–38 It is thought that this may be due to enhanced plaque vulnerability in non-culprit lesions, possibly as a consequence of pan-coronary inflammation.39 However, there are a number of issues that the trials do not resolve. Optimal timing of non-culprit artery treatment is uncertain since studies have involved either PCI during the index procedure, PCI during the index admission, or PCI during a later, planned hospital admission.36–38 There are other uncertainties in relation to the strategy of universal complete revascularisation in real world practice, including lack of mechanistic insight of benefit and variabilities in endpoint improvement (reduction in MI versus revascularization)40. For STEMI patients with cardiogenic shock, based on the results of the CULPRIT-SHOCK trial, multivessel PCI during the index procedure is not recommended.41 It is, however, noted that in the CULPRIT-SHOCK trial staged PCI of non-culprit lesions was encouraged(17.7% underwent PCI in the culprit only group), and therefore the strategy used is not too dissimilar from the “STEMI without cardiogenic shock” guidance.

*Antiplatelet therapy – prasugrel or ticagrelor?*

For STEMI, NICE recommended prasugrel in preference to ticagrelor.1 This was driven by the ISAR‑REACT 5 trial that directly compared ticagrelor and prasugrel in ACS patients.42 It is also consistent with UK observational data involving over 89000 primary PCI patients that showed an outcome advantage for prasugrel over ticagrelor.43 For NSTEMI, either prasugrel or ticagrelor is recommended. This is likely to be due to a variety of considerations including that neither was cost dominant and that practical difficulties could arise in using prasugrel because its licence does not support its use before angiography, which could leave people with unstable angina/NSTEMI without dual antiplatelet therapy for several days. There have been some criticisms on the reliability of the findings from the ISAR-REACT 5 trial including its open-label design (compared with double-blind TRITON-TIMI 38 and PLATO).44,45 Furthermore, instead of a direct comparison between drugs, the comparison was made between differing treatment strategies including preloading with ticagrelor but no preloading with prasugrel.42,44,45

**Summary**

The clinical guidelines on revascularisation described here offer a robust framework within which front line clinicians can plan the investigation and treatment of their patients. Inevitably, new evidence has the potential to render aspects of guidance obsolete. Table 4 highlights some of the recent landmark trials in myocardial revascularisation. Furthermore, there remains an important requirement for cardiologists to tailor their management strategy to each patient: especially because the majority of these would never have been suitable for inclusion into a randomised trial. Some gaps in our knowledge base may never be filled: a randomised trial of PCI versus OMT in significant left main disease, for example. In other areas, ongoing innovative research is highly likely to refine our understanding of optimal practice such as the identification of high-risk plaques in non-culprit STEMI disease.

**References**

1. National Institute for Health and Care Excellence. Acute coronary syndromes. 2020. https://www.nice.org.uk/guidance/ng185.

2. National Clinical Guidelines Centre. Stable angina: Full ( July 2011): methods, evidence & guidance. http://www.nice.org.uk/ guidance/cg126/evidence/fu.

3. Bangalore, S., Maron, D. J., Stone, G. W. & Hochman, J. S. Routine Revascularization Versus Initial Medical Therapy for Stable Ischemic Heart Disease: A Systematic Review and Meta-Analysis of Randomized Trials. *Circulation* **142**, 841–857 (2020).

4. Al-Lamee, R., Thompson, D., Dehbi, H.-M., Sen, S., Tang, K., Davies, J., Keeble, T., Mielewczik, M., Kaprielian, R., *et al.* Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. *Lancet (London, England)* **391**, 31–40 (2018).

5. Lawton, J. S., Tamis-Holland, J. E., Bangalore, S., Bates, E. R., Beckie, T. M., Bischoff, J. M., Bittl, J. A., Cohen, M. G., DiMaio, J. M., *et al.* 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* **145**, e4–e17 (2022).

6. Neumann, F.-J., Sousa-Uva, M., Ahlsson, A., Alfonso, F., Banning, A. P., Benedetto, U., Byrne, R. A., Collet, J.-P., Falk, V., *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur. Heart J.* **40**, 87–165 (2019).

7. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. Nice clinical guideline (2010). http://www. nice.org.uk/guidance/CG95.

8. HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography. [MTG32]. https://www.nice.org.uk/guidance/mtg32.

9. Curzen, N., Nicholas, Z., Stuart, B., Wilding, S., Hill, K., Shambrook, J., Eminton, Z., Ball, D., Barrett, C., *et al.* Fractional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain: the FORECAST randomized trial. *Eur. Heart J.* **42**, 3844–3852 (2021).

10. Douglas, P. S., Pontone, G., Hlatky, M. A., Patel, M. R., Norgaard, B. L., Byrne, R. A., Curzen, N., Purcell, I., Gutberlet, M., *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 s. *Eur. Heart J.* **36**, 3359–3367 (2015).

11. Knuuti, J., Wijns, W., Saraste, A., Capodanno, D., Barbato, E., Funck-Brentano, C., Prescott, E., Storey, R. F., Deaton, C., *et al.* 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur. Heart J.* **41**, 407–477 (2020).

12. Perera, D., Clayton, T., Petrie, M. C., Greenwood, J. P., O’Kane, P. D., Evans, R., Sculpher, M., Mcdonagh, T., Gershlick, A., *et al.* Percutaneous Revascularization for Ischemic Ventricular Dysfunction: Rationale and Design of the REVIVED-BCIS2 Trial: Percutaneous Coronary Intervention for Ischemic Cardiomyopathy. *JACC. Heart Fail.* **6**, 517–526 (2018).

13. Magnuson, E. A., Chinnakondepalli, K., Vilain, K., Serruys, P. W., Sabik, J. F., Kappetein, A. P., Stone, G. W. & Cohen, D. J. Cost-Effectiveness of Percutaneous Coronary Intervention Versus Bypass Surgery for Patients With Left Main Disease: Results From the EXCEL Trial. *Circ. Cardiovasc. Interv.* **15**, e011981 (2022).

14. Long-term results of prospective randomised study of coronary artery bypass surgery in stable angina pectoris. European Coronary Surgery Study Group. *Lancet (London, England)* **2**, 1173–1180 (1982).

15. Takaro, T., Peduzzi, P., Detre, K. M., Hultgren, H. N., Murphy, M. L., van der Bel-Kahn, J., Thomsen, J. & Meadows, W. R. Survival in subgroups of patients with left main coronary artery disease. Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease. *Circulation* **66**, 14–22 (1982).

16. Hueb, W., Lopes, N., Gersh, B. J., Soares, P. R., Ribeiro, E. E., Pereira, A. C., Favarato, D., Rocha, A. S. C., Hueb, A. C., *et al.* Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. *Circulation* **122**, 949–957 (2010).

17. Talano, J. V, Scanlon, P. J., Meadows, W. R., Kahn, M., Pifarre, R. & Gunnar, R. M. Influence of surgery on survival in 145 patients with left main coronary artery disease. *Circulation* **52**, I105-11 (1975).

18. Hueb, W., Soares, P. R., Gersh, B. J., César, L. A. M., Luz, P. L., Puig, L. B., Martinez, E. M., Oliveira, S. A. & Ramires, J. A. F. The medicine, angioplasty, or surgery study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: one-year results. *J. Am. Coll. Cardiol.* **43**, 1743–1751 (2004).

19. Yusuf, S., Zucker, D., Peduzzi, P., Fisher, L. D., Takaro, T., Kennedy, J. W., Davis, K., Killip, T., Passamani, E., *et al.* Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet (London, England)* **344**, 563–570 (1994).

20. Bittl, J. A., He, Y., Jacobs, A. K., Yancy, C. W. & Normand, S.-L. T. Bayesian methods affirm the use of percutaneous coronary intervention to improve survival in patients with unprotected left main coronary artery disease. *Circulation* **127**, 2177–2185 (2013).

21. Sabatine, M. S., Bergmark, B. A., Murphy, S. A., O’Gara, P. T., Smith, P. K., Serruys, P. W., Kappetein, A. P., Park, S.-J., Park, D.-W., *et al.* Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis. *Lancet (London, England)* **398**, 2247–2257 (2021).

22. Ahmad, Y., Howard, J. P., Arnold, A. D., Cook, C. M., Prasad, M., Ali, Z. A., Parikh, M. A., Kosmidou, I., Francis, D. P., *et al.* Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials. *Eur. Heart J.* **41**, 3228–3235 (2020).

23. Bangalore, S., Guo, Y., Samadashvili, Z., Blecker, S., Xu, J. & Hannan, E. L. Everolimus Eluting Stents Versus Coronary Artery Bypass Graft Surgery for Patients With Diabetes Mellitus and Multivessel Disease. *Circ. Cardiovasc. Interv.* **8**, e002626 (2015).

24. Thuijs, D. J. F. M., Kappetein, A. P., Serruys, P. W., Mohr, F.-W., Morice, M.-C., Mack, M. J., Holmes, D. R. J., Curzen, N., Davierwala, P., *et al.* Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *Lancet (London, England)* **394**, 1325–1334 (2019).

25. Head, S. J., Milojevic, M., Daemen, J., Ahn, J.-M., Boersma, E., Christiansen, E. H., Domanski, M. J., Farkouh, M. E., Flather, M., *et al.* Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. *Lancet (London, England)* **391**, 939–948 (2018).

26. Hueb, W. A., Bellotti, G., de Oliveira, S. A., Arie, S., de Albuquerque, C. P., Jatene, A. D. & Pileggi, F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. *J. Am. Coll. Cardiol.* **26**, 1600–1605 (1995).

27. Hueb, W. A., Soares, P. R., Almeida De Oliveira, S., Ariê, S., Cardoso, R. H., Wajsbrot, D. B., Cesar, L. A., Jatene, A. D. & Ramires, J. A. Five-year follow-op of the medicine, angioplasty, or surgery study (MASS): A prospective, randomized trial of medical therapy, balloon angioplasty, or bypass surgery for single proximal left anterior descending coronary artery stenosis. *Circulation* **100**, II107-13 (1999).

28. Hannan, E. L., Zhong, Y., Walford, G., Holmes, D. R. J., Venditti, F. J., Berger, P. B., Jacobs, A. K., Stamato, N. J., Curtis, J. P., *et al.* Coronary artery bypass graft surgery versus drug-eluting stents for patients with isolated proximal left anterior descending disease. *J. Am. Coll. Cardiol.* **64**, 2717–2726 (2014).

29. Aziz, O., Rao, C., Panesar, S. S., Jones, C., Morris, S., Darzi, A. & Athanasiou, T. Meta-analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery. *BMJ* **334**, 617 (2007).

30. Querdel, E., Reinsch, M., Castro, L., Köse, D., Bähr, A., Reich, S., Geertz, B., Ulmer, B., Schulze, M., *et al.* Human Engineered Heart Tissue Patches Remuscularize the Injured Heart in a Dose-Dependent Manner. *Circulation* **0**,.

31. Morice, M.-C., Serruys, P. W., Kappetein, A. P., Feldman, T. E., Ståhle, E., Colombo, A., Mack, M. J., Holmes, D. R., Choi, J. W., *et al.* Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation* **129**, 2388–2394 (2014).

32. Kofoed, K. F., Kelbæk, H., Hansen, P. R., Torp-Pedersen, C., Høfsten, D., Kløvgaard, L., Holmvang, L., Helqvist, S., Jørgensen, E., *et al.* Early Versus Standard Care Invasive Examination and Treatment of Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. *Circulation* **138**, 2741–2750 (2018).

33. Mehta, S. R., Granger, C. B., Boden, W. E., Steg, P. G., Bassand, J.-P., Faxon, D. P., Afzal, R., Chrolavicius, S., Jolly, S. S., *et al.* Early versus delayed invasive intervention in acute coronary syndromes. *N. Engl. J. Med.* **360**, 2165–2175 (2009).

34. Corcoran, D., Grant, P. & Berry, C. Risk stratification in non-ST elevation acute coronary syndromes: Risk scores, biomarkers and clinical judgment. *Int. J. Cardiol. Hear. Vasc.* **8**, 131–137 (2015).

35. Kite, T. A., Kurmani, S. A., Bountziouka, V., Cooper, N. J., Lock, S. T., Gale, C. P., Flather, M., Curzen, N., Banning, A. P., *et al.* Timing of invasive strategy in non-ST-elevation acute coronary syndrome: a meta-analysis of randomized controlled trials. *Eur. Heart J.* **43**, 3148–3161 (2022).

36. Wald, D. S., Morris, J. K., Wald, N. J., Chase, A. J., Edwards, R. J., Hughes, L. O., Berry, C. & Oldroyd, K. G. Randomized trial of preventive angioplasty in myocardial infarction. *N. Engl. J. Med.* **369**, 1115–1123 (2013).

37. Mehta, S. R., Wood, D. A., Storey, R. F., Mehran, R., Bainey, K. R., Nguyen, H., Meeks, B., Di Pasquale, G., López-Sendón, J., *et al.* Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N. Engl. J. Med.* **381**, 1411–1421 (2019).

38. Gershlick, A. H., Khan, J. N., Kelly, D. J., Greenwood, J. P., Sasikaran, T., Curzen, N., Blackman, D. J., Dalby, M., Fairbrother, K. L., *et al.* Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *J. Am. Coll. Cardiol.* **65**, 963–972 (2015).

39. Pinilla-Echeverri, N., Mehta, S. R., Wang, J., Lavi, S., Schampaert, E., Cantor, W. J., Bainey, K. R., Welsh, R. C., Kassam, S., *et al.* Nonculprit Lesion Plaque Morphology in Patients With ST-Segment-Elevation Myocardial Infarction: Results From the COMPLETE Trial Optical Coherence Tomography Substudys. *Circ. Cardiovasc. Interv.* **13**, e008768 (2020).

40. Mahmoudi, M. & Curzen, N. Treatment of Non-Culprit Lesions in STEMI: An Incomplete Journey. *Cardiovasc. Revasc. Med.* **39**, 114–116 (2022).

41. Thiele, H., Akin, I., Sandri, M., de Waha-Thiele, S., Meyer-Saraei, R., Fuernau, G., Eitel, I., Nordbeck, P., Geisler, T., *et al.* One-Year Outcomes after PCI Strategies in Cardiogenic Shock. *N. Engl. J. Med.* **379**, 1699–1710 (2018).

42. Schüpke, S., Neumann, F.-J., Menichelli, M., Mayer, K., Bernlochner, I., Wöhrle, J., Richardt, G., Liebetrau, C., Witzenbichler, B., *et al.* Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes. *N. Engl. J. Med.* **381**, 1524–1534 (2019).

43. Olier, I., Sirker, A., Hildick-Smith, D. J. R., Kinnaird, T., Ludman, P., de Belder, M. A., Baumbach, A., Byrne, J., Rashid, M., *et al.* Association of different antiplatelet therapies with mortality after primary percutaneous coronary intervention. *Heart* **104**, 1683–1690 (2018).

44. Wiviott, S. D., Braunwald, E., McCabe, C. H., Montalescot, G., Ruzyllo, W., Gottlieb, S., Neumann, F.-J., Ardissino, D., De Servi, S., *et al.* Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N. Engl. J. Med.* **357**, 2001–2015 (2007).

45. Wallentin, L., Becker, R. C., Budaj, A., Cannon, C. P., Emanuelsson, H., Held, C., Horrow, J., Husted, S., James, S., *et al.* Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N. Engl. J. Med.* **361**, 1045–1057 (2009).

**Figure 1 – Flowchart of NICE Stable Angina guidance**

****

**Figure 2 – Flow chart of NICE STEMI guidance**

**Figure 3 – Flowchart of NICE NSTEMI / Unstable guidance**

**Table 1 – Stable angina guidelines**

|  |  |  |
| --- | --- | --- |
| **NICE (2016)** | **ESC (2018 + 2019)** | **ACC / AHA / SCAI (2021)** |
| **Investigation** |  |  |
| ∙ CTCA if clinical assessment indicates typical or atypical angina, or if there are pathological ST segment or T-wave changes or Q waves on the resting ECG | ∙ Use of either non-invasive functional imaging of ischaemia or anatomical imaging using coronary CTCA as the initial test for diagnosing CAD | ∙ Among patients at intermediate-high risk and no known CAD, CCTA is useful for the diagnosis of CAD and for risk stratification; and stress imaging useful for the diagnosis of ischemia and for estimating the risk of MACE |
| ∙ Offer coronary angiography to guide treatment strategy for people with stable angina whose symptoms are not satisfactorily controlled with optimal medical treatment. Additional non-invasive or invasive functional testing may be required to evaluate angiographic findings and guide treatment decisions. | ∙ Invasive coronary angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood, severe symptoms refractory to medical therapy or typical angina at a low level of exercise, and clinical evaluation that indicates high event risk. (I B) | ∙ Coronary angiography is useful in patients with presumed SIHD who have unacceptable ischemic symptoms despite GDMT and who are amenable to, and candidates for, coronary revascularization. (I C)\* |
| **Revascularisation** |  |  |
| ∙ Consider revascularisation (coronary artery bypass graft [CABG] or percutaneous coronary intervention [PCI]) for people with stable angina whose symptoms are not satisfactorily controlled with optimal medical treatment | ∙ Revascularisation for stable angina / silent ischaemia: Haemodynamically significant coronary stenosis in the presence of limiting angina or angina equivalent (I A) with insufficient response to optimized medical therapy | ∙ In patients with refractory angina despite medical therapy and with significant coronary artery stenoses amenable to revascularisation, revascularisation is recommended to improve symptoms. (1 A) |
|  |
|  |
| ∙ Consider the relative risks and benefits of CABG and PCI for people with stable angina using a systematic approach to assess the severity and complexity of the patient's coronary disease, in addition to other relevant clinical factors and comorbidities | ∙ In patients with LM or multivessel disease, it is recommended that the SYNTAX score is calculated to assess the anatomical complexity of CAD and long-term risk of mortality and morbidity after PCI (I B); STS score recommended for surgical risk (I B); Euroscore II may be considered for surgical risk (II B) | ∙ If MVD, an assessment of CAD complexity, such as SYNTAX may be useful to guide revascularisation (2b B) |  |
|  |
|  |
| ∙ Offer PCI to patients with stable angina and suitable coronary anatomy when their symptoms are not satisfactorily controlled with optimal medical treatment AND revascularisation is considered appropriate AND CABG is not appropriate | ∙ More didactic based on SYNTAX score for left main CAD, 3VD (with or without diabetes mellitus) Also recommendations for Two vessel CAD, One vessel CAD with and without involvement of proximal LAD | ∙ More didactic based on disease complexity, presence of diabetes, left main and 3VD |  |
|  |
|  |
| ∙ Offer CABG to patients with stable angina and suitable coronary anatomy when symptoms not controlled AND revascularisation considered appropriate AND PCI is not appropriate | ∙ More didactic based on SYNTAX score for left main CAD, 3VD (with or without diabetes mellitus) Also recommendations for Two vessel CAD, One vessel CAD with and without involvement of proximal LAD | ∙ More didactic based on disease complexity, presence of diabetes, left main and 3VD |  |
|  |
|  |
| ∙ Consider CABG for people with stable angina and suitable coronary anatomy whose symptoms are satisfactorily controlled with optimal medical treatment, but coronary angiography indicates left main stem disease or proximal three-vessel disease. | ∙ More didactic based on SYNTAX score for left main CAD, 3VD (with or without diabetes mellitus) | ∙ Left main stenosis, CABG recommended to improve survival (1 B). |  |
|  |
|  |
| **Equipoise** |  |  |  |
| ∙ When either procedure would be appropriate, explain to the person the risks and benefits of PCI and CABG for people with anatomically less complex disease whose symptoms are not satisfactorily controlled with optimal medical treatment. If the person does not express a preference, take account of the evidence that suggests that PCI may be the more cost-effective procedure in selecting the course of treatment. | ∙ Not clearly mentioned. Importance of Heart Team stressed. (I C) | ∙ Not clearly mentioned. If optimal strategy unclear, a Heart Team approach is recommended to improve patient outcomes (1 B) |  |
|  |
|  |
| ∙ When either procedure appropriate, consider potential survival advantage of CABG if MVD with symptoms not satisfactorily controlled with optimal medical therapy and have diabetes OR are over 65 years OR have anatomically complex 3VD. with or without involvement of the left main stem | ∙ More didactic based on SYNTAX score for left main CAD, 3VD (with or without diabetes mellitus) | ∙ CABG reasonable to improve survival if complex MVD disease (e.g. SYNTAX >33) (2a B) and recommended if left main and complex disease to improve survival (1 B); If MVD and EF <35% CABG recommended (1 B); diabetic and MVD CABG recommended over PCI (1 A) |  |
|  |
|  |
| **MDT** |  |  |  |
| ∙ Ensure that there is a regular multidisciplinary team meeting to discuss the risks and benefits of continuing drug treatment or revascularisation strategy (CABG or PCI) for people with stable angina. | ∙ Heart Team (I C) | ∙ If optimal strategy unclear, a Heart Team approach is recommended to improve patient outcomes (1 B) |  |
|  |
|  |

\*2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease

**Table 2 – STEMI guidelines**

|  |  |  |
| --- | --- | --- |
| **NICE (2020)** | **ESC (2018)** | **ACC / AHA / SCAI (2021)** |
| ***Pharmacology*** |  |  |
| [∙ Prasugrel 1st line, as part of dual antiplatelet therapy with aspirin](https://www.medicines.org.uk/emc/product/6466/smpc) | ∙ Prasugrel or Ticagrelor (Ia) | ∙ Reasonable to use ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events, including stent thrombosis (2a B) |
|  |
|  |
| ∙ Clopidogrel with aspirin, if they are already taking an oral anticoagulant | ∙ Clopidogrel with indication for anticoagulation (IC) | ∙ If triple therapy, reasonable to choose clopidogrel in preference to prasugrel for triple therapy (IIa B)\* |  |
|  |
|  |
| ∙ Offer angiography ? PCI if presentation within 12 hours and PPCI delivered within 120minutes | ∙ PCI if < 120mins from STEMI diagnosis to wire crossing (I A) | [∙ In patients with STEMI and ischemic symptoms for <12 hours, PCI should be performed to improve survival. (1 A)](https://www.jacc.org/doi/10.1016/j.jacc.2021.09.006#bib183%20bib184%20bib185%20bib186%20bib187) |  |
|  |
|  |
| [∙ Offer unfractionated heparin with bailout glycoprotein IIb/IIIa inhibitor in combination with dual antiplatelet therapy to people with acute STEMI undergoing primary PCI with radial access.](https://www.nice.org.uk/guidance/ng185/chapter/recommendations#bailout-glycoprotein-iibiiia-inhibitor) | ∙ UFH is recommended (IC) | ∙ Glycoprotein Iib/IIIa inhibitor agents are reasonable to improve procedural success in patients with large thrombus burden, no-reflow or slow flow (2a C) |  |
|  |
|  |
| ∙ Consider bivalirudin with bailout glycoprotein IIb/IIIa inhibitor in combination with dual antiplatelet therapy for people with acute STEMI undergoing primary PCI when femoral access is needed. | ∙ Bivalirudin may be considered as an alternative to UFH (IIB) | ∙ In patients undergoing PCI, bivalirudin may be a reasonable alternative to UFH to reduce bleeding (2b A) |  |
|  |
|  |
| ***Revascularisation*** |  |  |  |
| ∙ Consider coronary angiography, with follow‑on primary PCI if presenting > 12 hours after the onset of symptoms if continuing myocardial ischaemia. | ∙ If > 12hours from symptoms, primary PCI indicated in presence of symptoms of ischaemia, haemodynamic instability or life-threatening arrhythmia (I C) | ∙ In patients with STEMI who are stable and presenting 12 to 24 hours after symptom onset, PCI is reasonable to improve clinical outcomes (2a B) |  |
|  |
|  |
| ∙ Consider radial arterial access | ∙ Radial over femoral if experience operator (IA) | ∙ Radial approach is indicated in preference to a femoral approach to reduce risk of death, vascular complications, or bleeding (1 A) |  |
|  |
|  |
| ∙ Do not routinely use mechanical thrombus extraction during primary PCI for people with acute STEMI. | ∙ Routine use of thrombus aspiration is not recommended (III A) | ∙ Routine aspiration thrombectomy before primary PCI is not useful (3 A) |  |
|  |
|  |
| ∙ Offer complete revascularisation without cardiogenic shock. Consider doing this during the index hospital admission. | ∙ Routine revascularisation of non-IRA lesions should be considered before hospital discharge (IIa A ) | ∙ In selected hemodynamically stable patients with STEMI and multivessel disease, after successful primary PCI, staged PCI of a significant non-infarct artery stenosis is recommended to reduce the risk of death or MI (1) |  |
|  |
|  |
| ∙ Consider culprit vessel only revascularisation during the index procedure if cardiogenic shock. | ∙ In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended during primary PCI. (III B) | ∙ In patients with STEMI complicated by cardiogenic shock, routine PCI of a non-infarct artery at the time of primary PCI should not be performed because of the higher risk of death or renal failure (3) |  |
|  |
|  |
| ∙ If stenting is indicated, offer a drug-eluting stent | ∙ New generation DES recommended over BMS for primary PCI (IA) | ∙ DES should be used in preference to BMS to prevent restenosis, MI or acute stent thrombosis (1 A) |  |
|  |
|  |
| ∙ Offer fibrinolysis to people with acute STEMI presenting within 12 hours of onset of symptoms if primary PCI cannot be delivered within 120 minutes | ∙ If time to PCI >120mins offer fibrinolysis strategy | ∙ Fibrinolytic therapy is recommended only in cases in which primary PCI is not immediately available and the delay from hospital presentation to PCI is anticipated to be >120minutes |  |
|  |
|  |
| ∙ Bailout angiogram if persistent ST elevation | ∙ Rescue PCI should be performed without delay in the case of unsuccessful fibrinolysis or within 2-24hours after bolus administration | [∙ In patients with STEMI and evidence of failed reperfusion after fibrinolytic therapy, rescue PCI of the infarct artery should be performed to improve clinical outcomes. (1 C)](https://www.jacc.org/doi/10.1016/j.jacc.2021.09.006#bib192%20bib193%20bib194%20bib195) |  |
|  |

**Table 3 – NSTEMI guidelines**

|  |  |  |
| --- | --- | --- |
| **NICE (2020)** | **ESC (2020)** | **ACC / AHA / SCAI (2021)** |
| **Risk stratification** |  |  |
| ∙ Assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6‑month mortality (for example, GRACE) | ∙ GRACE risk score models should be considered for estimating prognosis (Iia B) | ∙ GRACE score > 140 viewed as high risk and recommend an early invasive strategy within 24hours (2a B) |
| ∙ Consider conservative management without early coronary angiography for people with unstable angina or NSTEMI who have a low risk of adverse cardiovascular events (predicted 6‑month mortality 3.0% or less). | ∙ Selective invasive after appropriate ischaemia testing or detection of obstructive CAD by CTCA is recommended in low risk patients (I A) | ∙ In patients with NSTE-ACS who are initially stabilised and are at intermediate or low risk of clinical events, an invasive strategy with intent to perform revascularisation is reasonable before discharge to improve outcomes (2a B) |
| ∙ Consider coronary angiography (with follow‑on PCI if indicated) within 72 hours of first admission for people with unstable angina or NSTEMI who have an intermediate or higher risk of adverse cardiovascular events (predicted 6‑month mortality above 3.0%) | ∙ An early invasive strategy within 24 hours is recommended if any high risk criteria (I A) | ∙ In patients with NSTE-ACS who are initially stabilized and are at high risk of clinical events, it is reasonable to choose an early invasive strategy (within 24hours) over a delayed invasive strategy to improve outcomes (2a B) |
| ∙ Consider coronary angiography (with follow‑on PCI if indicated) for people with unstable angina or NSTEMI who are initially assessed to be at low risk of adverse cardiovascular events (predicted 6‑month mortality 3.0% or less) if ischaemia is subsequently experienced or is demonstrated by ischaemia testing. | ∙ Selective invasive after appropriate ischaemia testing or detection of obstructive CAD by CTCA is recommended in low risk patients (I A) | ∙ In patients with NSTE-ACS who are initially stabilised and are at intermediate or low risk of clinical events, an invasive strategy with intent to perform revascularisation is reasonable before discharge to improve outcomes (2a B) |
| ∙ Offer immediate coronary angiography to people with unstable angina or NSTEMI if their clinical condition is unstable. | ∙ An immediate strategy (<2hours) is recommended in patients with at least one of the very high risk criteria (I C) | ∙ In patients with NSTE-ACS and cardiogenic shock who are appropriate candidates for revascularisation, emergency revascularisation is recommended to reduce risk of death (1 B) |
| **Pharmacology** |  |  |
| ∙ Offer fondaparinux to people with unstable angina or NSTEMI who do not have a high bleeding risk unless they are undergoing immediate coronary angiography. | ∙ In case of medical treatment or logistical constraints for transferring the patient to PCI within the required time frame, fondaparinox is recommended and in such cases, a single bolus of UFH is recommended at the time of PCI (I B) | ∙ Fondaparinux: 2.5 mg SC daily, continued for the duration of hospitalization or until PCI is performed (I B)\*\* |
| ∙ For people with unstable angina or NSTEMI who are having coronary angiography, offer prasugrel or ticagrelor, as part of dual antiplatelet therapy with aspirin, if they have no separate indication for ongoing oral anticoagulation | ∙ Prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI (Iia B) | ∙ Reasonable to use ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events, including stent thrombosis (2a B) |
| ∙ Clopidogrel, as part of dual antiplatelet therapy with aspirin, if they have a separate indication for ongoing oral anticoagulation. | ∙ Aspirin and clopidogrel preferred in patients who require anticoagulation (I C) | ∙ If triple therapy, reasonable to choose clopidogrel in preference to prasugrel for triple therapy (IIa B)\* |
| **Revascularisation** |  |  |
| ∙ If stenting is indicated, offer a drug-eluting stent | ∙ DES recommended over BMS for any PCI (I A) | ∙ In patients undergoing PCI, DES should be used in preference to BMS to prevent restenosis, MI, or acute stent thrombosis (1 A) |
| ∙ When advising people with unstable angina or NSTEMI about the choice of revascularisation strategy (PCI or CABG), take account of coronary angiographic findings, comorbidities, and the benefits and risks of each intervention | ∙ Base revasc strategy on patient's clinical status and comorbidities, as well as their disease severity according to principles for stable CAD. However, decision on immediate PCI of the culprit stenosis does not require Heart Team consultation (I B) | ∙ Heart Team recommended (I B) |

\*\*2014 AHA/ACC NSTE-ACS \*2019 AHA/ACC/HRS focused update guideline for management of patients with atrial fibrillation

**Table 4: Summary of Recent Revascularisation Trials**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Trial** | **Date** | **Patients** | **Patient group** | **Design** | **Primary endpoint** | **Outcome** |
| **Stable Disease** |  |  |  |  |  |  |
| REVIVED-BCIS2 | 2022 | 700 | Stable patients with severe ischemic cardiomyopathy | PCI + OMT vs OMT | Primary composite outcome: death from any cause or hospitalization for heart failure | 37.2% PCI vs 38.0% OMT (p = 0.96). |
| ISCHEMIA | 2020 | 5179 | Stable coronary disease and moderate or severe ischemia | Initial invasive strategy + OMT vs OMT | Composite of CV death, MI, or hospitalization for unstable angina, heart failure, or cardiac arrest | 16.4% invasive and 18.2% conservative (p=NS) |
| ORBITA | 2018 | 230 | Stable angina with ischaemic symptoms | PCI + OMT vs Placebo + OMT | Difference in exercise time increment | PCI minus placebo: 16.6 s, 95% CI -8·9 to 42·0, p=0.200 |
| SYNTAXES | 2019 | 1800 | De-novo three-vessel and left main coronary artery disease (Angina or Asymptomatic myocardial ischaemia) | PCI vs CABG | 10 year all-cause death | 10 year all cause death: 28% PCI vs 24% CABG (p=0.066) |
| **ACS** |  |  |  |  |  |  |
| COMPLETE | 2019 | 4041 | STEMI and MVD | Culprit vs Complete Revasc | Cardiovascular death or myocardial infarction | 7.8% Complete vs 10.5% Culprit (p=0.004) |
| **Antiplatelet** |  |  |  |  |  |  |
| ISAR-REACT 5 | 2019 | 4018 | Acute Coronary Syndrome | Ticagrelor vs Prasugrel | Death, myocardial infarction, or stroke | 9.3% Ticagrelor vs 6.9% Prasugrel (p=0.006) |