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ESC/EACTS GUIDELINES

2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

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Abbreviations and acronyms

ABC	Age, Biomarkers, Clinical History
ABSORB II	A Bioresorbable Everolimus-Eluting Scaffold Versus a Metallic Everolimus-Eluting Stent II
AIDA	Amsterdam Investigator-Initiated Absorb Strategy All-Comers
ACCOAST	Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention or as Pretreatment at the Time of Diagnosis in Patients with Non-ST Elevation Myocardial Infarction
ACS	Acute coronary syndrome
ACUITY	Acute Catheterization and Urgent Intervention Triage strategy
ADAPT-DES	Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents
AF	Atrial fibrillation
ALPHEUS	Assessment of Loading With the $P2Y_{12}$-Inhibitor Ticagrelor or Clopidogrel to Halt Ischemic Events in Patients Undergoing Elective Coronary Stenting
AMI	Acute myocardial infarction
AMACING	A Maastricht Contrast-Induced Nephropathy Guideline
ANTARCTIC	Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an acute coronary syndrome
ARCTIC	Assessment by a Double Randomization of a Conventional Antiplatelet Strategy versus a Monitoring-guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption versus Continuation One Year after Stenting
ART	Arterial Revascularization Trial
AS	Aortic stenosis
ASE	American Society of Echocardiography
ATLANTIC	Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST-Elevation Myocardial Infarction to Open the Coronary Artery
ATLAS-ACS 2–TIMI 51	Anti-Xa Therapy to Lower cardiovascular events in Addition to Standard therapy in subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction 51
ATOLL	Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischaemic and bleeding events at short- and Long-term follow-up
AWESOME	Angina With Extremely Serious Operative Mortality Evaluation
BARC	Bleeding Academic Research Consortium
BARI-2D	Bypass Angioplasty Revascularization Investigation 2 Diabetes
BES	Biolimus-eluting stent
BEST	Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease
b.i.d.	Bis in die (twice daily)
BIMA	Bilateral internal mammary artery
BMS	Bare-metal stent
BRAVE	Bavarian Reperfusion Alternatives Evaluation
BRS	Bioresorbable scaffolds
BVS	Bioresorbable vascular scaffold
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CARDia	Coronary Artery Revascularization in Diabetes
CCS	Canadian Cardiovascular Society
CEA	Carotid endarterectomy
CHA_2DS_2-VASc	Cardiac Congestive heart failure, Hypertension, Age ≥75 [Doubled], Diabetes mellitus, prior Stroke or transient ischaemic attack or thromboembolism [Doubled] – Vascular disease, Age 65–74 and Sex category [Female]
CHAMPION	Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition
CI	Confidence interval
CIN	Contrast-induced nephropathy

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CKD	Chronic kidney disease
CMR	Cardiac magnetic resonance
COMPASS	Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease
COURAGE	Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
CPG	ESC Committee for Practice Guidelines
CT	Computed tomography
CT-FFR	CT-derived fractional flow reserve
CTO	Chronic total occlusion
CTSN	Cardiothoracic Surgical Trial Network
CULPRIT-SHOCK	Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock
CVA	Cerebrovascular accident
CvLPRIT	Complete Versus Lesion-Only Primary PCI Trial
DANAMI 3-DEFER	The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: DEFERred stent implantation in connection with primary PCI
DANAMI-3-PRIMULTI	The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: PRImary PCI in MULTIvessel Disease
DAPT	Dual antiplatelet therapy
DCB	Drug-coated balloon
DEFINE-FLAIR	Define Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularization
DES	Drug-eluting stents
DUS	Duplex ultrasound
EACTS	European Association for Cardio-Thoracic Surgery
EAPCI	European Association for Percutaneous Cardiovascular Interventions
EBC TWO	European Bifurcation Coronary TWO
ECG	Electrocardiogram
ECLS	Extracorporeal life support
ECMO	Extracorporeal membrane oxygenation
EES	Everolimus-eluting stent
EF	Ejection fraction
EMS	Emergency medical service
EROA	Effective regurgitant orifice area
ENTRUST-AF-PCI	Evaluation of the safety and efficacy of an edoxaban-based antithrombotic regimen in patients with atrial fibrillation following successful percutaneous coronary intervention
ESC	European Society of Cardiology
EUROCTO	Randomized Multicentre Trial to Compare Revascularization With Optimal Medical Therapy for the Treatment of Chronic Total Occlusions
EuroSCORE	European System for Cardiac Operative Risk Evaluation
EUROMAX	European Ambulance Acute Coronary Syndrome Angiography
EXCEL	Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization
FAME	Fractional Flow Reserve versus Angiography for Multivessel Evaluation
FDG-PET	Fluorodeoxyglucose positron emission tomography
FFR	Fractional flow reserve
FITT-STEMI	Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction
FMC	First medical contact
FREEDOM	Future Revascularization Evaluation in Patients with Diabetes Mellitus
GLOBAL LEADERS	Long-term ticagrelor monotherapy versus standard dual antiplatelet therapy followed by aspirin monotherapy in patients undergoing biolimus-eluting stent implantation
GP IIb/IIIa	Glycoprotein IIb/IIIa
GRAVITAS	Gauging Responsiveness with A VerifyNow assay-Impact on Thrombosis And Safety
HAS-BLED	Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol
HEAT-PPCI	How Effective are Antithrombotic Therapies in primary PCI
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HORIZONS	Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction
HPR	High platelet reactivity
HR	Hazard ratio
i.v.	Intravenous
IABP	Intra-aortic balloon pump
IABP-SHOCK II	Intraaortic Balloon Pump in Cardiogenic Shock II Trial
ICD	Implantable cardioverter defibrillator
iwFR	Instantaneous wave-free ratio
IMA	Internal mammary artery
IMR	Ischaemic mitral regurgitation
INR	International normalized ratio
IRA	Infarct-related artery
ISAR-CABG	Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts
ISAR-REACT	Intracoronary Stenting and Antithrombotic Regimen Rapid Early Action for Coronary Treatment
ISCHEMIA	International Study of Comparative Health Effectiveness With Medical and Invasive Approaches

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IVUS	Intravascular ultrasound imaging
LAA	Left atrial appendage
LAD	Left anterior descending
LEAD	Lower extremity artery disease
LGE-CMR	Late gadolinium enhancement cardiac magnetic resonance
LIMA	Left internal mammary artery
LM/LMS	Left main/left main stem
LMWH	Low-molecular-weight heparin
LPR	Low platelet reactivity
LV	Left ventricle/left ventricular
LVAD	Left ventricular assist device,
LVEF	Left ventricular ejection fraction
MACCE	Major adverse cardiac and cerebrovascular events
MACE	Major adverse cardiac events
MADIT II	Multicenter Automatic Defibrillator Implantation Trial II
MATRIX	Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX
MCS	Mechanical circulatory support
MI	Myocardial infarction
MINOCA	Myocardial infarction with non-obstructive coronary arteries
MLA	Minimal luminal area
MR	Mitral regurgitation
MSCT	Multi-slice computed tomography
MT	Medical therapy
MVD	Multivessel coronary artery disease
MVO	Microvascular obstruction
NAC	N-acetylcysteine
NNT	Number needed to treat
NOAC	Non-vitamin K antagonist oral anticoagulant
NOBLE	Nordic-Baltic-British Left Main Revascularization Study
NSTE-ACS	Non-ST-segment elevation acute coronary syndrome
NSTEMI	Non-ST-segment elevation myocardial infarction
NYHA	New York Heart Association
OAC	Oral anticoagulation
OASIS-5	Optimal Antiplatelet Strategy for Interventions-5
OCT	Optical coherence tomography
OR	Odds ratio
ORBITA	Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina
PARR-2	PET and Recovery following Revascularization
PCI	Percutaneous coronary intervention
Pd/Pa	Distal coronary to aortic pressure
PES	Paclitaxel-eluting stent
PET	Positron emission tomography
PF	Platelet function
PIONEER	Prevention of bleeding in patients with AF undergoing PCI
PLATFORM	Prospective LongitudinAl Trial of FFRct: Outcome and Resource Impacts,
PLATO	Study of Platelet Inhibition and Patient Outcomes
pLVAD	Percutaneous left ventricular assist device
p.o.	Per os (orally)
POSEIDON	Prevention of Contrast Renal Injury with Different Hydration Strategies
PPI	Proton pump inhibitor
PRAGUE-18	Comparison of Prasugrel and Ticagrelor in the Treatment of Acute Myocardial Infarction
PRAMI	Preventive Angioplasty in Acute Myocardial Infarction
PRECISE-DAPT	PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy
PRECOMBAT	Premier of Randomised Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease
PRESERVE	Prevention of Serious Adverse Events Following Angiography
q.d.	Quaque die (once daily)
RCT	Randomized controlled trial
RE-DUAL	Randomised Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patients with Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention
REMEDIAL II	Renal Insufficiency After Contrast Media Administration II
REPLACE-2	The Randomised Evaluation in PCI Linking Angiomax to Reduced Clinical Events 2
RIVAL	Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes
ROMA	Randomization of Single vs. Multiple Arterial Grafts
RR	Relative risk
SASSICAIA	Comparison of Loading Strategies With Antiplatelet Drugs in Patients Undergoing Elective Coronary Intervention
SAVR	Surgical aortic valve replacement
s.c.	Subcutaneous
SCAD	Stable coronary artery disease
SCD-HEFT	Sudden Cardiac Death in Heart Failure Trial
SES	Sirolimus-eluting stent
SHOCK	Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock
SIMA	Single internal mammary artery
SMART-DATE	Smart Angioplasty Research Team-safety of 6-month duration of Dual Antiplatelet Therapy after percutaneous coronary

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	intervention in patients with acute coronary syndromes
SPECT	Single-photon emission computed tomography
SR	Sinus rhythm
STEEPLE	Safety and Efficacy of Intravenous Enoxaparin in Elective Percutaneous Coronary Intervention Randomised Evaluation
STEMI	ST-segment elevation myocardial infarction
STICH	Surgical Treatment for Ischemic Heart Failure
STICHES	STICH Extension Study
STS	Society of Thoracic Surgeons
SVG	Saphenous vein graft
SVR	Surgical ventricular reconstruction
SWEDEHEART	Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies
SYNTAX	Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery
TAP	T and protrusion
TAVI	Transcatheter aortic valve implantation
TIA	Transient ischaemic attack
TIMI	Thrombolysis in Myocardial Infarction
TLR	Target lesion revascularization
TOTAL	Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI
TRIGGER-PCI	Testing platelet Reactivity In patients underGoing elective stent placement on clopidogrel to Guide alternative thErapy with pRasugrel
TRITON-TIMI 38	TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction
TROPICAL-ACS	Testing responsiveness to platelet inhibition on chronic antiplatelet treatment for acute coronary syndromes
TVR	Target vessel revascularization
TWILIGHT	Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention
UFH	Unfractionated heparin
VA	Veno-arterial
VACARDS	Veterans Affairs Coronary Artery Revascularization in Diabetes Study
VALIDATE	Bivalirudin versus Heparin in ST-Segment and Non–ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy
VKA	Vitamin K antagonist

1 Preamble

Clinical practice guidelines summarize and evaluate all available evidence at the time of the writing process on a particular issue with the aim of assisting physicians in selecting the best management strategies for an individual patient with a given condition, taking into account the impact on outcome as well as the risk–benefit ratio of particular diagnostic or therapeutic means. Clinical practice guidelines are no substitutes for textbooks, but complement them, and cover the European Society of Cardiology (ESC) Core Curriculum topics. As such they should help physicians to make decisions in their daily practice. However, final decisions should be individualized by responsible physicians and the patient.

A great number of clinical practice guidelines have been issued in recent years both by the ESC as well as by other societies and organizations. Because of the impact on clinical practice, quality criteria for the development of guidelines have been established in order to make all decisions transparent to the user. The recommendations for formulating and issuing ESC and joint society guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). These Guidelines represent the official position of the ESC and the European Association for Cardio-Thoracic Surgery (EACTS) on this given topic and will be regularly updated.

Members of this Task Force were selected by the ESC and EACTS to represent professionals involved with the medical care of patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for diagnosis, management (including treatment) and/or prevention of a given condition according to the ESC Committee for Practice Guidelines (CPG) and EACTS policy. A critical evaluation of diagnostic and therapeutic procedures was performed including assessment of the risk–benefit ratio. Estimates of expected health outcomes for larger populations were included, where data exist. The level of evidence and the strength of recommendation of particular treatment options were weighed and graded according to predefined scales, as outlined in *Tables 1 and 2*.

The experts of the writing and reviewing panels completed declarations of interest forms on what might be perceived as real or potential sources of conflicts of interest. These forms were compiled into one file and can be found on the ESC and EACTS websites http://www.escardio.org/guidelines and http://www.eacts.org). Any changes in declarations of interest that arise during the writing period must be notified to the ESC and EACTS and updated. The Task Force received its entire financial support from the ESC and EACTS without any involvement from the healthcare industry.

The CPG-ESC and EACTS supervised and coordinated the preparation of these new Guidelines produced by the joint Task Force. These entities are also responsible for the endorsement process of these Guidelines. The ESC/EACTS Guidelines underwent extensive review by a wide panel of relevant external experts. After appropriate revisions it was approved by all the experts involved in the Task Force. The finalized document was approved by the ESC CPG and EACTS for joint publication in the *European Heart Journal* and the *European Journal of Cardio-Thoracic Surgery*.

The task of developing clinical practice guidelines covers not only the integration of the most recent research, but also the creation of educational tools and implementation programmes for the recommendations. To implement the guidelines, condensed pocket guidelines, summary slides, booklets with essential messages, and an electronic version for digital applications (smartphones, etc.) are produced. These versions are abridged and, thus, if needed, one should

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Table 1 Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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Table 2 Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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always refer to the full text version, which is freely available on the ESC and EACTS websites. The National Societies of the ESC are encouraged to endorse, translate, and implement the ESC Guidelines. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.

Surveys and registries are needed to verify that real-life daily practice is in keeping with what is recommended in the guidelines, thus completing the loop between clinical research, writing of guidelines, and implementing them in clinical practice.

The guidelines do not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

2 Introduction

These Guidelines represent the third time that the ESC and EACTS have brought together cardiologists and cardiac surgeons in a joint Task Force to review the ever-increasing body of evidence, with the mission of drafting balanced, patient-centred practice Guidelines on myocardial revascularization. Summaries of the key changes in comparison with the previous Guidelines are provided in *Figures 1 and 2*.

There is considerable overlap of the current document with other Guidelines, specifically those on stable coronary artery disease, non-ST-elevation myocardial infarction, ST-elevation myocardial infarction, heart failure, valvular heart disease and the Focused Update on Dual Antiplatelet Therapy. Unless supported by new evidence, we followed the recommendations of these Guidelines where pertinent to our Guidelines, and refer the reader to the respective sections in those documents for detailed discussion. We reserve more in-depth discussion for topics that are specific to issues pertaining to myocardial revascularization that are not covered in other Guidelines. To keep the current document concise and reader-friendly, we also moved some of the detailed descriptions of study results to the online Supplementary Data.

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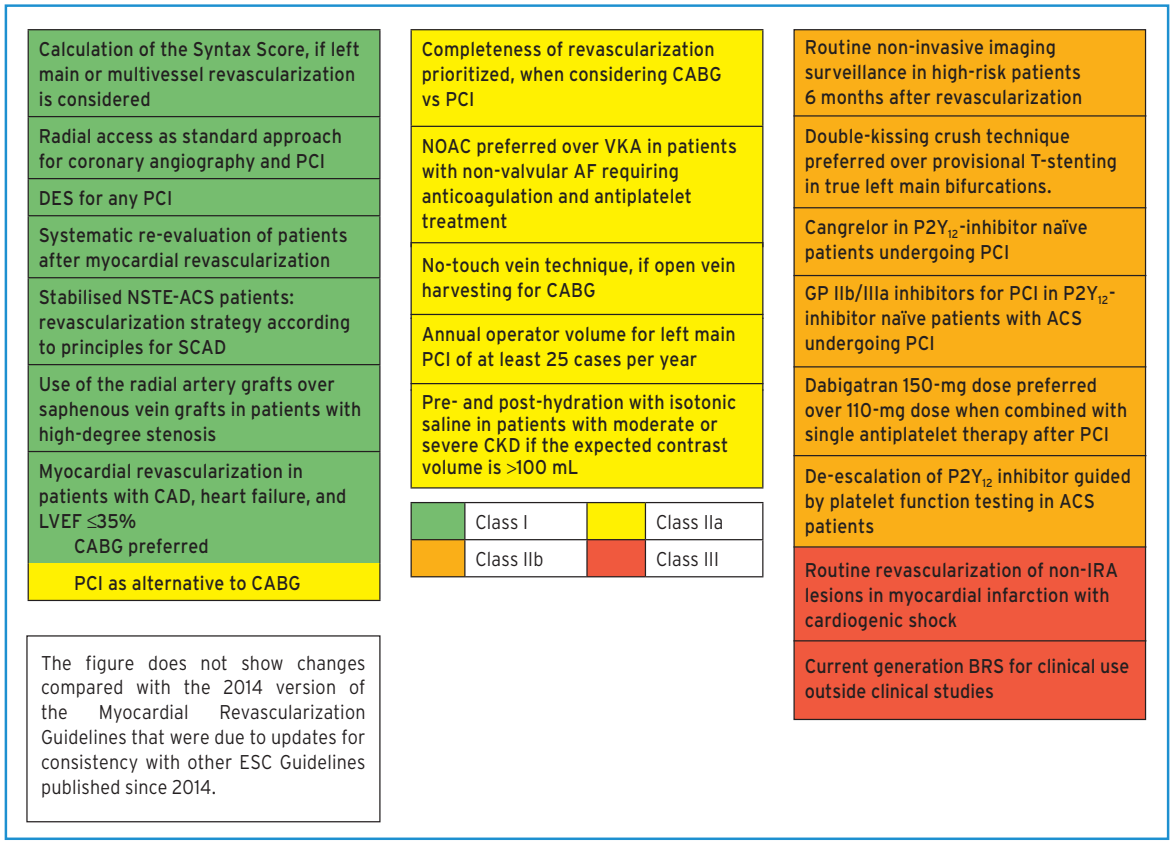
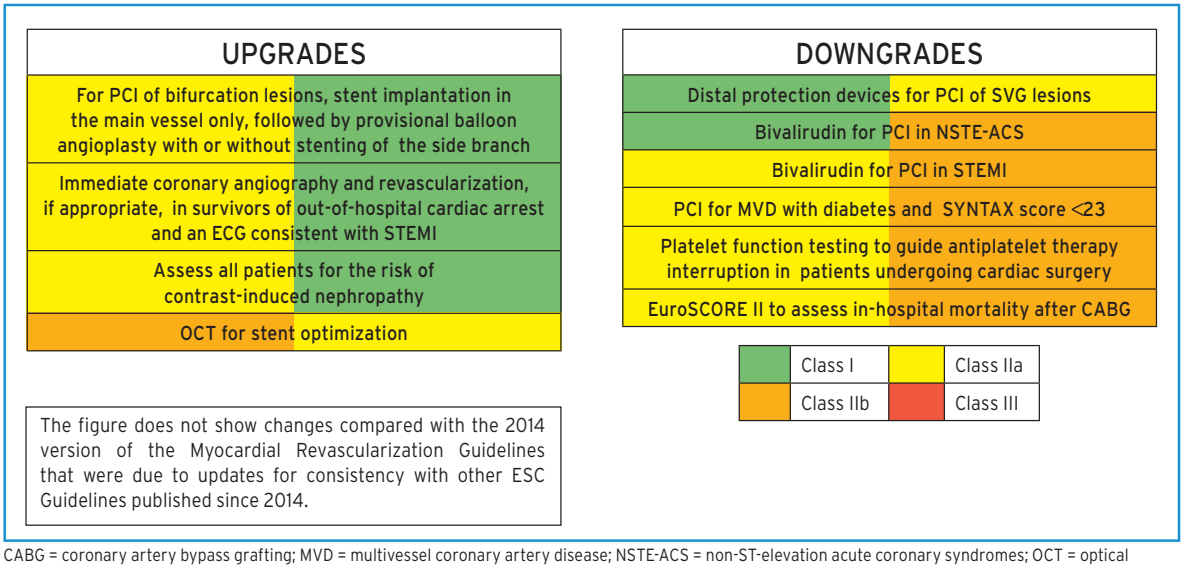
2.1 What is new in the 2018 Guidelines?



ACS = acute coronary syndromes; AF = atrial fibrillation; BRS = bioresorbable scaffolds; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CKD = chronic kidney disease; DES = drug-eluting stents; FFR = fractional flow reserve; GP = glycoprotein; IRA = infarct-related artery; LVEF = left ventricular ejection fraction; NOAC = non-vitamin K oral anticoagulants; NSTEMI = non-ST-elevation; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; VKA = vitamin K antagonists.

Figure 1 New recommendations.



CABG = coronary artery bypass grafting; MVD = multivessel coronary artery disease; NSTE-ACS = non-ST-elevation acute coronary syndromes; OCT = optical coherence tomography; PCI = percutaneous coronary interventions; STEMI = ST-elevation myocardial infarction, SVG = saphenous vein grafts;

Figure 2 Changes in class of recommendation.

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3 Diagnostic tools to guide myocardial revascularization

The use of diagnostic imaging and functional testing modalities to detect patients with coronary artery disease (CAD) is discussed in detail in the clinical practice Guidelines for patients with SCAD.[1] Further diagnostic assessment of patients with obstructive CAD is critical in order to identify patients and select specific lesions that are likely to benefit from myocardial revascularization, in addition to optimal medical therapy.

3.1 Non-invasive diagnostic tools

3.1.1 Assessment of myocardial ischaemia

Non-invasive diagnostic assessment of patients with CAD being considered for myocardial revascularization comprises the assessment of ischaemia and the evaluation of viability in patients with regional wall motion abnormalities or reduced ejection fraction (EF).

Functional testing to assess ischaemia is critical for the assessment of stable patients with CAD. Documentation of ischaemia using functional testing before elective invasive procedures for CAD is the preferred approach. It may also have a role in the assessment of some patients presenting with acute coronary syndrome (ACS). Because of the low sensitivity of exercise electrocardiogram (ECG) testing in the assessment of patients with symptoms of angina, non-invasive imaging is recommended as the first-line test.[1] Detection of a large area of myocardial ischaemia by functional imaging is associated with impaired prognosis of patients and identifies patients who should undergo revascularization (see section 5).

In patients undergoing coronary computed tomography (CT), both CT-derived fractional flow reserve (CT-FFR) and CT perfusion represent possible approaches to evaluate lesion-specific ischaemia. Although the evidence for both is limited at present, there are considerably more data from clinical investigations of CT-FFR. A number of trials have shown that correlation between CT-derived FFR and invasive FFR is high.[2,3] The non-randomized PLATFORM (Prospective LongitudinAl Trial of FFRct: Outcome and Resource Impacts) study showed that in patients referred for invasive angiography due to chest pain (predominantly atypical angina) and intermediate pre-test probability of CAD, assessment with CT and CT-FFR reduced the number of patients with subsequently normal invasive coronary angiograms compared with standard care.[4] Currently, clinical trial data with CT-FFR are insufficient to make a recommendation for its use in clinical practice.

3.1.2 Assessment of myocardial viability in patients with heart failure and coronary artery disease

In patients with regional wall motion abnormalities or ventricular dysfunction, heart failure (HF) can be caused by stunned or hibernating myocardium and may be reversed by revascularization. Assessment of myocardial viability may be done in order to select patients that are more likely to benefit from myocardial revascularization and can be achieved with several imaging modalities: myocardial contrast echocardiography, single-photon emission CT (SPECT), and late gadolinium enhancement cardiac magnetic resonance (LGE-CMR) all assess cellular integrity; positron emission tomography (PET) assesses cellular metabolism; and dobutamine techniques assess contractile reserve.[1,5] Assessment of ischaemia provides incremental benefit over viability in mild to moderate CAD, but with extensive CAD viability assessment may be sufficient.[6] Patients with advanced HF and viable myocardium should first undergo revascularization with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) before being considered for mechanical circulatory support (MCS) or heart transplantation.[7,8]

The PARR-2 (PET and Recovery following Revascularization) trial included patients with severe left ventricular (LV) dysfunction being considered for revascularization or HF/transplantation workups, and randomized them to management assisted by fluorodeoxyglucose PET (FDG-PET) or standard care.[6] The primary outcome of cardiac death, myocardial infarction (MI), or recurrent hospital stay for cardiac cause at 1 year was not improved in the group managed by FDG-PET [relative risk (RR) 0.82, 95% confidence interval (CI) 0.59–1.14, $P = 0.16$], though the rate of compliance with the treatment recommended by FDG-PET was variable.

The viability substudy of the STICH (Surgical Treatment for Ischemic Heart Failure) trial found viable myocardium in 487/601 patients (81%) and none in 114 (19%).[9] There was a significant association between myocardial viability and outcome by univariate analysis, but not on multivariable analysis. The lack of correlation between myocardial viability and benefit from revascularization indicates that this strategy should not be the only test when selecting the optimal therapy.

Recommendations for non-invasive imaging in patients with coronary artery disease and heart failure with reduced ejection fraction

Recommendations	Class[a]	Level[b]
Non-invasive stress imaging (CMR, stress echocardiography, SPECT, or PET) may be considered for the assessment of myocardial ischaemia and viability in patients with HF and CAD (considered suitable for coronary revascularization) before the decision on revascularization.[9–11]	IIb	B

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CAD = coronary artery disease; CMR = cardiac magnetic resonance; HF = heart failure; PET = positron emission tomography; SPECT = single-photon emission computed tomography.
[a]Class of recommendation.
[b]Level of evidence.

3.2 Invasive diagnostic tools

3.2.1 Pressure-derived fractional flow reserve

3.2.1.1 Use of fractional flow reserve in patients with intermediate-grade coronary stenosis including left main stenosis

Coronary pressure-derived FFR is the current standard of care for the functional assessment of lesion severity in patients with intermediate-grade stenosis (typically around 40 – 90% stenosis) without evidence of ischaemia in non-invasive testing, or in those with multivessel disease.

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Multiple studies have shown that PCI can be safely deferred if FFR is >0.75.[12–15] The DEFER trial enrolled 325 patients scheduled for PCI of an intermediate stenosis.[15] If FFR was ≥0.75, patients were randomly assigned to deferral (defer group; *n* = 91) or performance (perform group; *n* = 90) of PCI. The composite rate of cardiac death and acute MI (AMI) in the defer and perform groups was 3.3 vs. 7.9% (*P* = 0.21).

However, most contemporary studies use an FFR cut-off of 0.80. A recent large-scale observational study supports the use of FFR >0.80 rather than 0.75 as a cut-off.[16] Indeed, the two largest studies in this field, DEFINE-FLAIR (Define Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularization DES drug-eluting stent)[17] and iFR-SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies),[18] used the 0.80 cut-off for lesion selection by FFR, with favourable event rates at 1 year. Thus, 0.80 is the accepted FFR threshold for defining haemodynamically relevant lesions.

Haemodynamic relevance, as defined by FFR ≤0.80, correlates poorly with diameter stenosis by visual assessment. In the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) trial, only 35% of the 50–70% stenoses were haemodynamically relevant and, of the 71–90% stenoses, 20% were not. Only an estimated diameter stenosis >90% predicted haemodynamic relevance with high accuracy (96% correct classification). A number of studies have shown that utilization of an FFR-based assessment strategy at the time of angiography results in reclassification of the revascularization strategy (PCI, bypass surgery, or medical therapy) in a high proportion of patients with intermediate-grade lesions (>40% of patients are reclassified).[19–22] In addition, separate and pooled analyses of the patients included in those studies have shown that the end results of 'FFR-based reclassification' in patients investigated at the time of diagnostic angiography is neutral overall for the number of patients indicated for revascularization.[23]

A patient-level and study-level meta-analysis of 9173 lesions demonstrated that with lesions with FFR <0.75, revascularization reduced the 1 year risk of major adverse cardiac events (MACE), including a reduction in the composite risk of death and MI.[24] Thus, the FFR threshold of 0.75 is used to define more severe ischaemia that is of prognostic relevance.

The presence of intermediate grade left main stem (LMS) disease is not infrequent and angiographic evaluation may be challenging. Assessment using pressure-derived FFR is more challenging in comparison with non-LMS stenosis due to the requirement for disengagement of the guiding catheter and an inability to administer intracoronary adenosine. Some observational data exist to support the use of FFR in order to decide if revascularization should be deferred or performed.[25] In the largest study, which included 230 patients with intermediate-grade LMS stenosis, only 23% showed an FFR <0.80. Treatment was deferred in patients with an FFR ≥0.80 and bypass surgery was done in patients with an FFR <0.80.[26] Clinical outcomes at 5 years were similar in both groups. However, it is important to consider the potential influence of any untreated downstream disease in the left anterior descending (LAD) or left circumflex arteries, which may be associated with an increased risk of a false negative FFR.[27]

The value of FFR to evaluate intermediate stenosis and guide selection of lesions for revascularization at the time of bypass surgery has been shown in an observational study.[28] Of the 627 patients with intermediate stenosis that were evaluated, 429 had bypass without FFR and 198 had bypass with FFR; in the latter group, the proportion of patients with three-vessel disease was reclassified from 94 to 86%. Outcomes were similar in both groups at 3 years [hazard ratio (HR) for death/MI/target vessel revascularization (TVR) = 1.03, 95% CI 0.67–1.69], though the group with FFR guidance was associated with a lower number of graft anastomoses and a lower rate of on-pump surgery compared with angiography-guided CABG surgery.

3.2.1.2 Use of fractional flow reserve to identify lesions requiring revascularization in patients with multivessel coronary artery disease undergoing percutaneous coronary intervention

FFR may also be useful for the selection of lesions requiring revascularization in patients with multivessel CAD. The FAME trial showed that in patients with multivessel disease randomized to an FFR-guided PCI strategy (using a cut-off ≤0.80 to indicate requirement for PCI), outcomes at 12 months in terms of death, non-fatal MI, and repeat revascularization were superior compared with angiography-guided PCI and utilized fewer resources.[29] In addition, the 2 year composite risk of death or MI was significantly lower with the FFR-guided PCI strategy.[30] Long-term follow-up at 5 years showed broadly consistent findings, although differences between groups in relation to the primary endpoint were no longer significant.[31] This suggests that FFR-guided PCI should be the preferred management strategy in these patients.

3.2.1.3 Fractional flow reserve-guided management vs. medical therapy in patients with coronary artery disease

In patients with SCAD and at least one stenosis with FFR ≤0.80, the FAME 2 trial showed that PCI using drug-eluting stent (DES) implantation improved the primary endpoint of death, non-fatal MI, or urgent revascularization within 2 years compared with medical treatment alone, which was driven by a lower need for urgent revascularization.[32] The advantage of FFR-guided PCI over medical therapy alone was maintained at 3 years.[33]

3.2.2 Other pressure-derived indices

FFR evaluation requires maximal and stable hyperaemia, which is usually obtained by the administration of intravenous (i.v.) adenosine. Recently, there has been renewed interest in resting indices derived from resting gradients alone [distal coronary to aortic pressure (Pd/Pa) or instantaneous wave-free ratio (iwFR)]. Two recent large-scale randomized trials showed broadly comparable results between FFR-guided and iwFR-guided revascularization strategies in patients with intermediate-grade stenosis.[17,18] Revascularization was indicated in both trials if FFR was ≤0.80 or if iwFR was ≤0.89. In the DEFINE-FLAIR trial, the primary endpoint of MACE at 1 year occurred in 6.8% in patients randomized to iwFR-guided revascularization vs. 7.0% in patients randomized to FFR-guided revascularization (*P* <0.001 for non-inferiority; HR 0.95, 95% CI 0.68–1.33, *P* = 0.78).[17] In the iFR-SWEDEHEART trial, the primary endpoint of death from any cause, non-fatal MI, or unplanned revascularization was 6.7% in the iwFR group and 6.1% in the FFR group (*P* = 0.007 for non-inferiority; HR 1.12, 95% CI 0.79–1.58, *P* = 0.53).[18] In this trial, 17.5% of patients had ACS at the time of presentation. There was no interaction with outcomes. Both trials are limited by having a follow-up duration of only 1 year.

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The SYNTAX II study (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery), a single-arm, prospective study in patients with multivessel disease incorporating a management strategy including combined iwFR/FFR assessment of stenosis severity in addition to intravascular ultrasound (IVUS)-guided stent implantation and guideline-directed medical therapy, showed encouraging outcomes compared with a historical cohort enrolled in the SYNTAX trial.[34]

Randomized trials comparing iwFR-guided revascularization with angiography-guided revascularization or medical therapy are not available. iwFR has not been extensively validated for patients with LMS stenosis.

There is no adequate randomized controlled trial (RCT) data to support the use of whole-cardiac cycle Pd/Pa for the guidance of revascularization decisions.

3.2.3 Use of fractional flow reserve and pressure-derived indices in patients with severe aortic stenosis

In patients with intermediate coronary stenosis and concomitant severe aortic stenosis, although some observational studies exist (see section 11), there are no adequate RCT data to support the use of FFR or iwFR for the guidance of revascularization decisions.

3.2.4 Use of intravascular imaging for the diagnostic assessment of stenosis

IVUS is an ultrasound-based modality of intravascular imaging with an axial resolution of about 150 μm. IVUS imaging allows real-time tomographic assessment of vessel size, lumen area, and plaque composition and volume. In comparison with optical coherence tomography (OCT), it has more limited spatial resolution, but better penetration depth and potential advantages in terms of vessel sizing. OCT is a light-based modality of intravascular imaging with higher axial resolution compared with IVUS (15 vs. 150 μm). The disadvantages of OCT imaging are that it requires complete blood clearance from the lumen for imaging and that it has more limited penetration, which can limit the assessment of complete plaque burden and may impair accurate vessel sizing.

Potential clinical uses of intravascular imaging for diagnostic assessment in patients being considered for myocardial revascularization are the evaluation of stenosis severity in lesions with intermediate-grade stenosis, evaluation of lesion morphology in lesions ambiguous with angiographic assessment, and the characterization of plaque composition. The majority of the existing data from clinical trials relate to the use of intravascular imaging guidance during PCI and are discussed in section 16. The use of intravascular imaging to evaluate patients with stent failure is discussed in section 13.

Regarding the assessment of intermediate-grade stenosis, a number of studies have evaluated the optimal cut-off of minimal lumen area for the identification of haemodynamically relevant lesions. One prospective registry showed overall moderate correlation of minimal lumen area with FFR values, with cut-off values for detecting haemodynamically relevant stenosis (<2.4, <2.7, and <3.6 mm2) dependent on vessel size (reference vessel diameters <3.0, 3.0–3.5, and >3.5 mm, respectively).[34a] Generally, haemodynamic assessment with FFR should be preferred for this indication.

The presence of intermediate-grade LMS disease is not infrequent and angiographic assessment may be challenging. Assessment using IVUS evaluation of intermediate-grade LMS disease in patients being considered for bypass surgery or PCI is supported by data from a number of observational studies.[35–38] In a multicentre, prospective study, revascularization was mainly deferred if the minimal luminal area (MLA) was ≥6 mm^2 and performed in cases of an MLA <6 mm^2.[37] After a 2 year follow-up, cardiac death-free survival was similar in both groups (98 and 95%, respectively). Another study suggested that deferral of intervention in 131 patients with an MLA ≥7.5 mm^2 showed favourable clinical outcomes.[36] In Asian patients with generally smaller heart sizes, studies have suggested that an IVUS MLA of 4.5–4.8 mm^2 may be the most appropriate.[38]

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

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FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

3.3 Gaps in the evidence

Further studies investigating the role of novel, combined, non-invasive anatomical and functional imaging are needed, such as randomized clinical trials with CT-FFR in patients with suspected and known CAD, as well as further clinical investigation of perfusion CT.

Randomized trials comparing iwFR-based management of patients with intermediate-grade stenosis compared with medical therapy are missing. Further study of whole-cardiac cycle Pd/Pa for the guidance of revascularization in the setting of randomized clinical trials is also required.

Further studies including randomized trials are needed to assess the value of functional vs. anatomical guidance for CABG.

4 Process for decision-making and patient information

4.1 Patient information and informed consent

Informed consent requires transparency, especially if there is debate over various treatment options. Active patient participation in the

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decision-making process should be encouraged. Patient information needs to be unbiased, evidence-based, up-to-date, reliable, accessible, relevant, and consistent with legal requirements. Use of terminology that the patient understands is essential. Short-term procedure-related and long-term risks and benefits—such as survival, relief of angina, quality of life, the potential need for late reintervention, the need for prevention measures, and uncertainties associated with different treatment strategies—should be thoroughly discussed. Although current recommendations are mostly based on the ability of treatments to reduce adverse events including mortality, there is growing interest in patient-reported outcome measures.[40,41] Patients are not only interested to know how recommended treatment impacts on prognosis but also on their quality of life in the way they perceive it. A written evidence-based patient information document should be provided, potentially with decision aids.

Patients must have the time to reflect on the trade-offs imposed by the outcome estimates. In order to seek a second opinion or to discuss the findings and consequences with referring physicians, enough time should be allowed—up to several days, as required—between diagnostic catheterization and intervention. These recommendations pertain to patients in a stable condition, for whom various treatment options exist and who can make a decision without the constraints of an urgent or emergent situation (*Table 3*). The patient's right to decline the treatment option recommended by the Heart Team has to be respected. Patient refusal of a recommended treatment should be acknowledged in a written document after the patient has received the necessary information by the Heart Team members. In this case, the patient may be offered an alternative treatment option by the Heart Team.

The patient has the right to obtain information on the level of expertise of the operator, the workload of the centre, whether all treatment options—including surgery—are available on-site, and local results in the performance of percutaneous and surgical myocardial revascularization procedures. Patients considered for revascularization should also be clearly informed of the continuing need for medical therapy, as well as lifestyle modification and other secondary prevention strategies (see section 19).[42]

4.2 Multidisciplinary decision-making (Heart Team)

The Heart Team—comprising clinical or non-invasive cardiologists, cardiac surgeons, and interventional cardiologists, as well as anaesthetists and other specialists if deemed necessary—should provide a balanced, multidisciplinary decision-making process.[43] Additional input may be needed from other specialties involved in the care of the patient. The Heart Team should meet on a regular basis to analyse and interpret the available diagnostic evidence, determine the need for myocardial revascularization, and assess the relative short- and long-term safety and effectiveness of the percutaneous and surgical options. *Ad hoc* meetings of the Heart Team should facilitate and support efficient clinical workflows.

The need for an interdisciplinary approach is underlined by reports on (i) the underuse of revascularization procedures in 18–40% of patients with CAD[44] and (ii) inappropriate use of revascularization strategies with a lack of case discussions.[45] The marked variability in PCI-to-CABG ratios between European countries (ranging from 2.4–7.6 in 2013, for example) has raised concerns regarding the appropriate selection of revascularization strategies.[46] Rates for the inappropriate use of PCI (10–15%)[43,47,48] and CABG (1–2%) are reported. Multidisciplinary decision-making in a Heart Team can minimize specialty bias and prevent self-referral from interfering with optimal patient care.[49]

Several reports from different centres have established that the treatment recommendations made in multidisciplinary Heart Team discussions are reproducible and implemented in the vast majority of cases (93–95%).[50,51]

Interdisciplinary institutional protocols should be developed for common case scenarios to avoid the need for systematic case-by-case review of all diagnostic angiograms. However, complex cases—defined by the protocols—should be discussed individually. In these cases, revascularization should not be performed at the time of diagnostic angiography, to allow sufficient time to assess all available information and clearly explain and discuss the findings with the patient. The rationale for a decision and consensus on the optimal revascularization treatment should be documented on the patient's chart. In institutions without an on-site cardiac surgery unit, collaboration with an external cardiac surgery unit is required to design protocols that define when Heart Team discussion is needed.

4.3 Timing of revascularization

Patients requiring myocardial revascularization may be at increased risk of adverse events during the waiting period.[52] A recent meta-analysis of observational studies calculated that a waiting period of 3 months for surgical myocardial revascularization may be associated with the risk of 1 death among 80 patients.[53] *Table 3* shows the preferred timing of revascularization depending on the clinical presentation and the extent and localization of CAD.[54] Sections 7 and 8 show additional and more specific information in this regard for patients with ACS.

Ad hoc PCI is defined as a therapeutic intervention performed within the same procedure as the diagnostic coronary angiography. *Ad hoc* PCI is convenient, often cost-effective and safe, and is associated with fewer access site complications and lower radiation exposure.[55,56] However, in the USA, up to 30% of patients undergoing *ad hoc* PCI are potential candidates for CABG.[56] This number may be lower in Europe.[45] Although it is not advisable for *ad hoc* PCI to represent the default approach for complex SCAD, it may be justified if a full diagnostic work-up, including functional testing, is available and the patient is adequately informed on both percutaneous and surgical myocardial revascularization options (see section 4.1). Institutional protocols developed by the Heart Team in accordance with current Guidelines should define specific anatomical criteria and clinical subsets that may be—or should not be—treated *ad hoc*. Stable patients with complex CAD, as reflected by a high SYNTAX score, should in general be discussed by the Heart Team and not be treated *ad hoc*.

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Table 3 **Multidisciplinary decision pathways, patient informed consent, and timing of revascularization**

	ACS				
	Shock	**STEMI**	**NSTE-ACS**	**SCAD without *ad hoc* PCI indication according to Heart Team protocol**	**SCAD with *ad hoc* PCI indication according to Heart Team protocol**
Multidisciplinary decision-making	Not mandatory during the acute phase; mechanical circulatory support according to Heart Team protocol	Not mandatory during the acute phase	Not mandatory during the acute phase; after stabilization, recommended as in SCAD	Required	Not required
Informed consent	Witnessed verbal informed consent or family consent if possible without delay	Witnessed verbal informed consent may be sufficient unless written consent is legally required	Written informed consent[a]; in emergency cases witnessed verbal informed consent may be sufficient	Written informed consent[a]	Written informed consent[a]
Time to revascularization	Emergency: no delay	Emergency: no delay	Urgency: within 2 h to within 72 h depending on the risk criteria	Within 2 weeks for high-risk patients[b] and within 6 weeks for all other patients	*Ad hoc*
Procedure	Proceed with intervention based on best evidence/availability. *Ad hoc* treatment of culprit lesion, staged treatment of non-culprit lesions according to institutional protocol or Heart Team decision.	Proceed with intervention based on best evidence/availability. Non-culprit lesions treated according to institutional protocol or Heart Team decision.	Proceed with intervention based on best evidence/availability. Non-culprit lesions treated according to institutional protocol or Heart Team decision.	Allow for enough time from diagnostic catheterization to decide on the appropriate intervention.	Proceed with intervention according to institutional protocol defined by Heart Team.

ACS = acute coronary syndromes; CCS = Canadian Cardiovascular Society; ESC = European Society of Cardiology; EACTS = European Association for Cardio-Thoracic Surgery; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; STEMI = ST-segment elevation myocardial infarction.

[a]This may not apply to countries that are not legally required to ask for written informed consent. The ESC and EACTS advocate the documentation of patient consent for all revascularization procedures.

[b]Severe symptoms (CCS class 3), anatomy (left main disease or equivalent, three-vessel disease or proximal left anterior descending artery), or depressed ventricular function.

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Recommendations for decision-making and patient information in the elective setting

Recommendations	Class[a]	Level[b]
It is recommended that patients undergoing coronary angiography are informed about benefits and risks, as well as potential therapeutic consequences, ahead of the procedure.	I	C
It is recommended that patients are adequately informed about short- and long-term benefits and risks of the revascularization procedure with information about local experience, and allowed enough time for informed decision-making.	I	C
It is recommended that institutional protocols are developed by the Heart Team to implement the appropriate revascularization strategy in accordance with current Guidelines.	I	C
In PCI centres without on-site surgery, it is recommended that institutional protocols are established with partner institutions providing cardiac surgery.	I	C

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PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

5 Revascularization for stable coronary artery disease

5.1 Rationale for revascularization

The indications for revascularization in patients with SCAD who receive guideline-recommended medical treatment are the persistence of symptoms despite medical treatment and/or the improvement of prognosis.[1]

Several studies have shown that myocardial revascularization by PCI or CABG more effectively relieves angina, reduces the use of anti-anginal drugs, and improves exercise capacity and quality of life compared with a strategy of medical therapy alone during short- and long-term follow-up (Supplementary *Table 1*).[32,33,57–62] Recently, the ORBITA (Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina) trial randomly compared PCI with placebo (sham procedure) in patients with SCAD due to single-vessel CAD (diameter stenosis >70%) and preserved LV function in the presence of moderate symptoms of angina [Canadian Cardiovascular Society (CCS) class II in 59% of patients, duration 9 months] for the first time.[63] After 6 weeks of medication optimization (mean number of anti-anginal drugs: 3) and baseline cardiopulmonary exercise testing, 200 patients were randomized (105 PCI and 95 placebo). Following a 6-week post-randomization period, the primary endpoint of increment in exercise time was not significantly different, but estimates were imprecise (PCI minus placebo 16.6 sec, 95% CI −8.9 to 42.0, $P = 0.20$). The dobutamine stress echocardiography peak stress wall motion score index improved with PCI (-0.09, 95% CI -0.15 to -0.04, $P = 0.001$). ORBITA raises the issue of whether the symptom relief of PCI in the specific setting of stable single-vessel CAD may be related at least in part to a placebo effect. Limitations of the study, as acknowledged by the investigators and outlined elsewhere, include the short observation period (6 weeks), the inclusion of patients with mild symptoms pre-randomization (CCS class 0-I in 25% of patients), the group imbalance in ostial and proximal lesions (37 vs. 57%, $P = 0.005$), loss to follow-up after randomization, and the insufficient power to detect a true difference.[64] This precludes definite conclusions at this stage. Nevertheless, the ORBITA study underlines the value of optimal medical therapy in the management of SCAD.

Three year follow-up of the FAME 2 study indicated yearly and sustained improvement of angina (10.2 vs. 28.5% at 1 month and 5.2 vs. 9.7% at 3 years) in favour of FFR-guided PCI, despite considerable crossover in the medical therapy arm.[33] Among patients with multivessel disease, the assessment of frequency of angina and quality of life measures in the SYNTAX, FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus), and EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trials consistently showed early and sustained improvement for both PCI and CABG during long-term follow-up.[65–67]

5.2 Evidence basis for revascularization

The indications for revascularization in patients with stable angina or silent ischaemia are summarized in the recommendation table.

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Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class[a]	Level[b]
For prognosis	Left main disease with stenosis >50%.[c] [68–71]	I	A
	Proximal LAD stenosis >50%.[c] [62,68,70,72]	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%).[c] [61,62,68,70,73–83]	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR.[d] [24,59,84–90]	I	B
	Single remaining patent coronary artery with stenosis >50%.[c]	I	C
For symptoms	Haemodynamically significant coronary stenosis[c] in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy.[e] [24,63,91–97]	I	A

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CAD = coronary artery disease; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LAD = left anterior descending coronary artery; LV = left ventricular; LVEF = left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.
[c]With documented ischaemia or a haemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89 (see section 3.2.1.1), or >90% stenosis in a major coronary vessel.
[d]Based on FFR <0.75 indicating a prognostically relevant lesion (see section 3.2.1.1).
[e]In consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy.

5.2.1 Revascularization with the use of percutaneous coronary intervention

Several meta-analyses comparing a strategy of PCI with initial medical therapy among patients with SCAD found no or only modest benefits in terms of survival or MI for an invasive strategy, taking into account the fact that up to 40% of patients crossed over after to revascularization during longer-term follow-up.[91,98,99] A network meta-analysis of 100 trials with 93 553 patients and 262 090 patient-years of follow-up comparing a strategy of initial medical therapy with revascularization reported improved survival using PCI with new-generation DES (everolimus: rate ratio 0.75, 95% CI 0.59–0.96; zotarolimus: rate ratio 0.65, 95% CI 0.42–1.00) compared with initial medical treatment.[100]

In the FAME 2 trial,[32] patients with SCAD and at least one functionally significant stenosis (invasive FFR ≤0.80) were randomly assigned to medical therapy or medical therapy plus FFR-guided PCI using new-generation DES. The 3 year report of the FAME 2 trial reported a lower incidence of the primary composite endpoints of death, MI, and urgent revascularization (10.1 vs. 22.0%; P <0.001), driven by a lower incidence of urgent revascularization in the PCI group (4.3 vs. 17.2%; P <0.001) and without significant differences in the rates of death and MI.[33] At 2 years of follow-up, the rate of death or MI was lower in the PCI than the medical therapy group (4.6 vs. 8.0%; HR 0.56, 95% CI 0.32–0.97, P = 0.04) in a landmark analysis between 8 days and 2 years of follow-up, whereas event rates were higher during days 0 - 7 due to periprocedural MI (for overview of studies see Supplementary *Table 2*).[97]

5.2.2 Revascularization with the use of coronary artery bypass grafting

The superiority of CABG over a strategy of initial medical therapy was established in a meta-analysis of seven RCTs[68] more than two decades ago, demonstrating a survival benefit of CABG in patients with SCAD and left main (LM) or three-vessel disease, particularly when the proximal LAD coronary artery was involved, and has been corroborated in more recent studies.[100,101] A network meta-analysis of 100 trials with 93 553 patients comparing a strategy of initial medical therapy with revascularization reported improved survival (RR 0.80, 95% CI 0.63–0.99) and a reduced risk of MI (RR 0.79, 95% CI 0.83–0.99) among patients undergoing CABG compared with initial medical treatment.[100]

In the STICH trial, 1212 patients with CAD and an LV ejection fraction (LVEF) ≤35% were randomized to initial medical therapy or CABG. The extended 10 year follow-up of the STICH trial reported a significant reduction in all-cause (59 vs. 66%; HR 0.84, 95% CI 0.73–0.97; P = 0.02) and cardiovascular mortality (41 vs. 49%; HR 0.79, 95% CI 0.66–0.93; P = 0.006).[81] For an overview of studies, see Supplementary *Table 2*.

5.3 Percutaneous coronary intervention vs. coronary artery bypass grafting

The recommendations for the type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality are summarized below. The Heart Team should take into consideration the individual cardiac and extracardiac characteristics, in addition to patient preference, in the overall decision-making process (*Figure 3*). A summary of trials comparing the outcomes of patients treated with angioplasty vs. CABG and bare-metal stent (BMS) vs. CABG is shown in Supplementary *Table 3*, and of studies comparing DES and CABG in *Table 4*.

5.3.1 Criteria for decision-making

Predicted surgical mortality, the anatomical complexity of CAD, and the anticipated completeness of revascularization are important criteria for decision-making with respect to the type of revascularization

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Table 4 Randomized clinical trials comparing percutaneous coronary intervention with drug-eluting stents vs. surgical revascularization

Stent type and year of publication	Study	N	Baseline characteristics					Primary endpoint[a]			Secondary endpoints[a]				
			Age (y)	Women (%)	Diabetes (%)	MV disease (%)	EF (%)	Definition	Y	Results	Y	Death	MI	Revasc	Stroke
DES															
PES 2009	SYNTAX[102]	1800	65	22	25	MV 61 LM 39	-	Death, MI, stroke, or repeat revasc	1	17.8 vs. 12.4%	5	13.9 vs. 11.4%	9.7 vs. 3.8%*	25.9 vs. 13.7%*	2.4 vs. 3.7%
SES 2011	Boudriot[103]	201	68	25	36	LM 100	65	Death, MI, or repeat revasc	1	13.9 vs. 19%	1	2 vs. 5%	3 vs. 3%	14 vs. 5.9%	-
SES 2011	PRECOMBAT[104]	600	62	24	32	LM 100	61	Death, MI, stroke, or TVR	1	8.7 vs. 6.7%[b]	2	2.4 vs. 3.4%	1.7 vs. 1.0%	9.0 vs. 4.2%*	0.4 vs. 0.7%
EES 2015	BEST[105]	880	64	29	41	MV 100	60	Death, MI, or TVR	2	11.0 vs. 7.9%	5	6.6 vs. 5.0%	4.8 vs 2.7%	13.4 vs. 6.6%	2.9 vs. 3.3%
BES 2016	NOBLE[106]	1201	66	22	15	LM 100	60	Death, MI, or TVR	5	15.4 vs. 7.2%	5	11.6 vs. 9.5%	6.9 vs. 1.9%*[c]	16.2 vs. 10.4%*	4.9 vs. 1.7%
EES 2016	EXCEL[107]	1905	66	24	30	LM 100	57	Death, MI, or stroke	3	15.4 vs. 14.7%[b]	3	8.2 vs. 5.9%	8.0 vs. 8.3%	13.4 vs. 6.6%*	2.3 vs. 2.9%

Age and EF are reported as means.
*P <0.05.
BES = biolimus-eluting stents; BEST = Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease; DES = drug-eluting stents; EES = everolimus-eluting stent; EF = ejection fraction; EXCEL = Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; LM = left main coronary artery disease; MI = myocardial infarction; MV = multivessel coronary artery disease; NOBLE = Nordic-Baltic-British Left Main Revascularization Study; PES = paclitaxel-eluting stents; PRECOMBAT = Premier of Randomised Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; Revasc = revascularization; SES = sirolimus-eluting stents; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; TVR = target vessel revascularization; Y = years.
[a]Results are reported as percutaneous coronary intervention vs. coronary artery bypass grafting.
[b]Non-inferiority met.
[c]Non-procedural MI (exclusion of periprocedural MI).

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(CABG or PCI). Whether conservative therapy, PCI, or CABG is preferred should depend on the risk-benefit ratios of these treatment strategies, weighing up the risks of periprocedural complications (e.g. cerebrovascular events, blood transfusions, renal failure, new onset arrhythmias, or wound infections) against improvements in health-related quality of life, as well as long-term freedom from death, MI, or repeat revascularization.

5.3.1.1 Predicted surgical mortality

To assess the predicted surgical mortality, the European System for Cardiac Operative Risk Evaluation (EuroSCORE II) (www.euroscore.org/calc.html) and the Society of Thoracic Surgeons (STS) score (http://riskcalc.sts.org) were both developed based on clinical variables to estimate the operative in-hospital or 30 day mortality risk[108–110] (Supplementary *Table 4*). Both scores have demonstrated their value in specific cohorts of patients undergoing CABG.[111] Calibration of the STS score is updated on a regular basis. It has been suggested that the STS score outperforms the EuroSCORE II when compared directly in a cohort of CABG patients,[112] although other studies have found comparable performance of both models.[113,114]

There are no established cut-offs for low predicted surgical mortality based on the EuroSCORE II or STS score. Thus, individualized treatment decisions are needed. These decisions should respect the range of predicted surgical risks in the major RCTs that inform the choice of revascularization modality (*Table 5*). In these studies, the predicted surgical risk was assessed by the logistic EuroSCORE. Compared with the more recent EuroSCORE II, the logistic EuroSCORE has similar discrimination but poorer calibration and, thus, overestimates surgical mortality by roughly two-fold.[115]

Despite the usefulness of these scores, there is not a single risk model that provides perfect risk assessment because the scores are limited by (i) the specific definitions used or the methodology applied, (ii) the absence of important variables such as frailty, (iii) the practicability of calculation, (iv) a failure to reflect all relevant mortality and morbidity endpoints, and (v) limited external validation. Decision-making should not be solely dependent on risk scores. These scores should be used as a guide within the multidisciplinary Heart Team discussion.

To combine clinical and anatomical risk estimation, the SYNTAX II score was retrospectively derived from the SYNTAX cohort[127] and subsequently externally validated.[120,128,129] Nevertheless, compared with the SYNTAX score, its value in assigning patients to PCI or CABG is less well investigated. The fact that the SYNTAX II score failed to predict the outcome of the EXCEL trial raises additional concern.[130]

5.3.1.2 Anatomical complexity of coronary artery disease

The SYNTAX score (http://www.syntaxscore.com) was prospectively developed for the SYNTAX trial to grade the anatomical complexity of coronary lesions in patients with LM or three-vessel disease (*Table 6* and Supplementary *Table 4*).[116] In the cohort of the SYNTAX trial, and subsequently in external validation cohorts, the SYNTAX score was found to be an independent predictor of long-term major adverse cardiac and cerebrovascular events (MACCE) and of death in patients treated with PCI but not CABG.[117–120]

In the SYNTAX trial, tertiles of SYNTAX score with low, intermediate, and high anatomical complexity stratified patients into those who had similar outcomes with both PCI and CABG and those who derived significant benefit from CABG.[121–123] In subsequent RCTs, the interaction of the strata of SYNTAX score with the effect of the randomized treatment was less pronounced and did not reach statistical significance.[105–107] However, in a recent collaborative individual patient pooled analysis of randomized trials including 11 518 patients,[124] the test for trend across the ordered tertiles of the SYNTAX score of the SYNTAX study was positive at $P = 0.0011$ (unpublished analysis), confirming the strata of the SYNTAX score as an effect modifier to be considered. There is concern about bias and inter-individual variability in calculating the SYNTAX score.[125] This should be minimized by adequate training.

Table 5 Logistic EuroSCOREs in major randomized trials comparing percutaneous coronary intervention with coronary artery bypass grafting

Trial	EuroSCORE PCI	EuroSCORE CABG
SYNTAX	3.8 ± 2.6	3.8 ± 2.7
BEST	2.9 ± 2.0	3.0 ± 2.1
FREEDOM	2.7 ± 2.4	2.8 ± 2.5
PRECOMBAT	2.7 ± 1.8	2.8 ± 1.9
EXCEL	Not reported	Not reported
NOBLE	2 (2–4)	2 (2–4)

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Numbers are presented as mean ± SD or median (interquartile range).
BEST = Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease; CABG = coronary artery bypass grafting; EuroSCORE = European System for Cardiac Operative Risk Evaluation; EXCEL = Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; NOBLE = Nordic-Baltic-British Left Main Revascularization Study; PCI = percutaneous coronary intervention; PRECOMBAT = Premier of Randomised Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.

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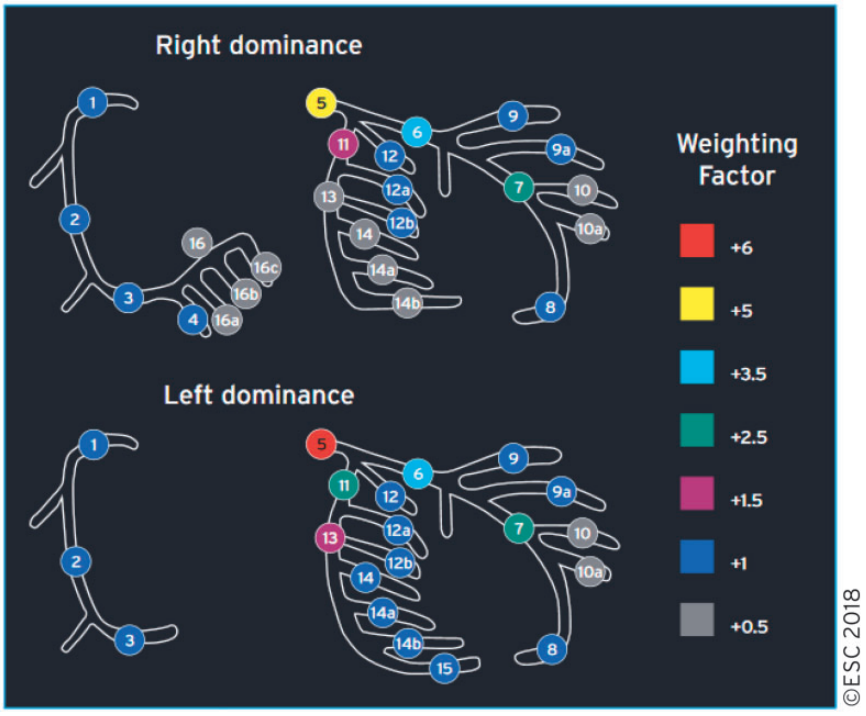
Table 6 Guide for calculating the SYNTAX score

Steps	Variable assessed	Description
Step 1	Dominance	The weight of individual coronary segments varies according to coronary artery dominance (right or left). Co-dominance does not exist as an option in the SYNTAX score.
Step 2	Coronary segment	The diseased coronary segment directly affects the score as each coronary segment is assigned a weight depending on its location, ranging from 0.5 (i.e. the posterolateral branch) to 6 (i.e. left main in case of left dominance). 
Step 3	Diameter stenosis	The score of each diseased coronary segment is multiplied by two in case of a stenosis 50–99% and by five in case of total occlusion. In case of total occlusion, additional points will be added as follows: • Age >3 months or unknown +1 • Blunt stump +1 • Bridging +1 • First segment visible distally +1 per non-visible segment • Side branch at the occlusion +1 if <1.5 mm diameter +1 if both <1.5 mm and ≥1.5 mm diameter +0 if ≥1.5 mm diameter (i.e. bifurcation lesion)
Step 4	Trifurcation lesion	The presence of a trifurcation lesion adds additional points based on the number of diseased segments: • 1 segment +3 • 2 segments +4 • 3 segments +5 • 4 segments +6

Continued

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Step 5	Bifurcation lesion	The presence of a bifurcation lesion adds additional points based on the type of bifurcation according to the Medina classification:[126] • Medina 1,0,0–0,1,0–1,1,0 +1 • Medina 1,1,1–0,0,1–1,0,1–0,1,1 +2 Moreover, the presence of a bifurcation angle <70° adds one additional point
Step 6	Aorto-ostial lesion	The presence of aorto-ostial lesion segments adds one additional point
Step 7	Severe tortuosity	The presence of severe tortuosity proximal of the diseased segment adds two additional points
Step 8	Lesion length	Lesion length >20 mm adds one additional point
Step 9	Calcification	The presence of heavy calcification adds two additional points
Step 10	Thrombus	The presence of thrombus adds one additional point
Step 11	Diffuse disease/ small vessels	The presence of diffusely diseased and narrowed segments distal to the lesion (i.e. when at least 75% of the length of the segment distal to the lesion has a vessel diameter <2 mm) adds one point per segment number

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SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.

5.3.1.3 Completeness of revascularization

The aim of myocardial revascularization is to minimize residual ischaemia. In support of this concept, the nuclear substudy of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial demonstrated an incremental benefit in reducing the risk of death and MI by reducing residual stress-induced ischaemia from >10% of the myocardium to ≤5%.[86]

In the SYNTAX trial, anatomical complete revascularization was defined as PCI or bypass of all epicardial vessels with a diameter exceeding ≥1.5 mm and a luminal reduction of ≥50% in at least one angiographic view.[131] A meta-analysis of 89 883 patients enrolled in RCTs and observational studies revealed a lower long-term mortality (RR 0.71, 95% CI 0.65–0.77, *P* <0.001), MI (RR 0.78, 95% CI 0.68–0.90; *P* = 0.001), and repeat myocardial revascularization (RR 0.74, 95% CI 0.65–0.83; *P* <0.001) by complete revascularization (based on anatomical definition in 87% of the patients) as compared with incomplete revascularization.[132] The benefit of complete revascularization was independent of the treatment modality. A more recent meta-analysis suggested enhanced benefit when complete revascularization is performed with state-of-the-art techniques in high-risk patients.[133] Likewise, in a *post hoc* analysis of the SYNTAX trial, anatomical incomplete revascularization was associated with inferior long-term outcomes after both CABG and PCI.[131] A residual SYNTAX score >8 after PCI was associated with significant increases in the 5-year risk of death and of the composite of death, MI, and stroke, and any residual SYNTAX score >0 was associated with the risk of repeat intervention.[134] In an observational study from the New York State registry that compared CABG with PCI using new-generation DES [everolimus-eluting stent (EES)] in 9223 pairs of propensity-matched patients with multivessel CAD, the significantly higher risk of MI associated with PCI as compared with CABG was not seen among matched pairs of patients in which the PCI group had complete revascularization ($P_{interaction}$ = 0.02).[135] Consistent findings were obtained in a pooled analysis of 3212 patients of the SYNTAX, BEST (Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease), and PRECOMBAT (Premier of Randomised Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trials.[136] A mean SYNTAX score of 27 and an LVEF of 59% were obtained. In a propensity-matched analysis, mortality and the composite risk of death, MI, and stroke were significantly lower after PCI with complete vs. incomplete revascularization. After PCI with complete revascularization, the risk of death or of the composite of death, MI, or stroke was not significantly different from that after CABG with complete revascularization (adjusted HR 1.16, 95% CI 0.83–1.63, *P* = 0.39, and 1.14, 95% CI 0.87–1.48, *P* = 0.35, respectively), whereas these risks were significantly elevated after PCI with incomplete revascularization.

Functional complete revascularization is achieved when all lesions causing resting or stress-induced ischaemia are bypassed or treated by PCI. Given the limitations of non-invasive imaging techniques (see section 3), these lesions are identified by FFR or iwFR during diagnostic angiography. For PCI, the FAME study demonstrated that the more restrictive selection of target lesions by functional guidance conferred superior long-term outcomes compared with anatomically guided lesion selection (see section 3).[31] In contrast, leaving functionally relevant lesions untreated resulted in a high rate of reinterventions in the FAME 2 study.[33] Based on the data of the FAME and FAME 2 studies, complete revascularization based on the functional definition is the preferred strategy for PCI.

The role of functional guidance for CABG is less clear.[28,137] One of the potential benefits of CABG is protection against disease progression in proximal segments, which may be diminished by restricting the bypass targets to functionally relevant lesions. This has to be weighed against the risk of bypass closure when native vessel flow is high. Thus, for ambiguous lesions, functional testing may also help guide the surgical revascularization strategy.

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Recommendations on criteria for the choice between coronary artery bypass grafting and percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Assessment of surgical risk[c]		
It is recommended that the STS score is calculated to assess in-hospital or 30 day mortality, and in-hospital morbidity after CABG.[112,114,138]	I	B
Calculation of the EuroSCORE II score may be considered to assess in-hospital mortality after CABG.[112]	IIb	B
Assessment of CAD complexity		
In patients with LM or multivessel disease, it is recommended that the SYNTAX score is calculated to assess the anatomical complexity of CAD and the long-term risk of mortality and morbidity after PCI.[117–124]	I	B
When considering the decision between CABG and PCI, completeness of revascularization should be prioritized.[131,132,134–136]	IIa	B

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EuroSCORE = European System for Cardiac Operative Risk Evaluation; CABG = coronary artery bypass grafting; CAD = coronary artery disease; LM = left main; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.
[a]Class of recommendation.
[b]Level of evidence.
[c]Level of evidence refers to prediction of outcomes.

Recommendation for the type of revascularization in patients with stable coronary artery disease with suitable coronary anatomy for both procedures and low predicted surgical mortality[d]

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
One-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,101,139–144]	I	A	I	A
Two-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,70,73]	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145–148]	I	A	I	A
Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145–148]	I	A	IIa	A
Left main disease with high SYNTAX score (≥33).[c] [69,121,122,124,146–148]	I	A	III	B
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score (0 - 22).[102,105,121,123,124,135,149]	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c] [102,105,121,123,124,135,149]	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0–22.[102,105,121,123,124,135,150–157]	I	A	IIb	A
Three-vessel disease with intermediate or high SYNTAX score (>22).[c] [102,105,121,123,124,135,150–157]	I	A	III	A

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SYNTAX score calculation information is available at http://www.syntaxscore.com.
CABG = coronary artery bypass grafting; CAD = coronary artery disease; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.
[a]Class of recommendation.
[b]Level of evidence.
[c]PCI should be considered if the Heart Team is concerned about the surgical risk or if the patient refuses CABG after adequate counselling by the Heart Team.
[d]For example, absence of previous cardiac surgery, severe morbidities, frailty, or immobility precluding CABG (also see *Table 5*).

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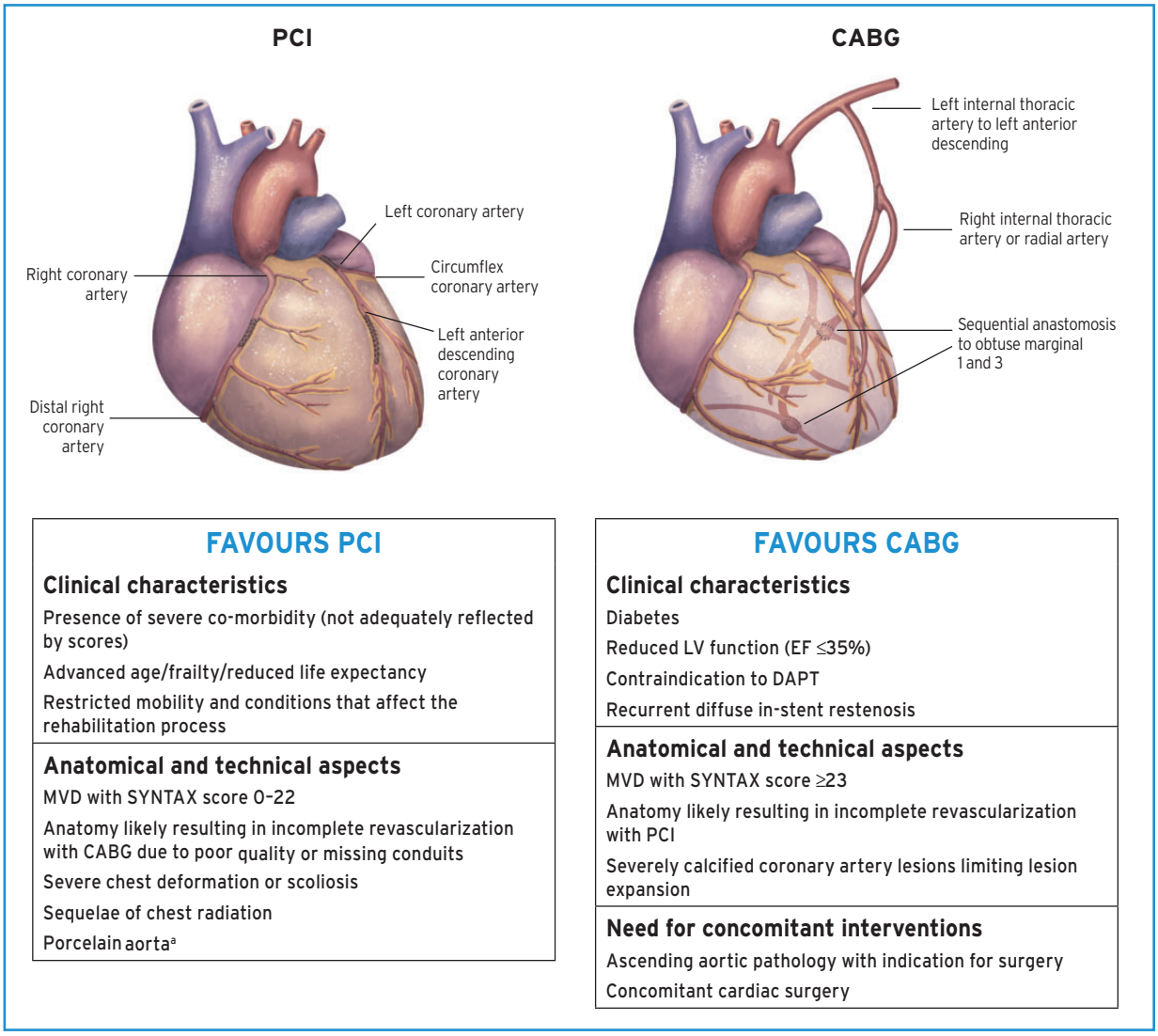

CABG = coronary artery bypass grafting; Cx = circumflex; DAPT = dual antiplatelet therapy; EF = ejection fraction; LAD = left anterior descending coronary artery; LIMA = left internal mammary artery; LV= left ventricular; MVD = multivessel coronary artery disease; PCI = percutaneous coronary intervention; PDA = posterior descending artery; RA = radial artery; RIMA = right internal mammary artery; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.
[a]Consider no-touch off-pump CABG in case of porcelain aorta.

Figure 3 Aspects to be considered by the Heart Team for decision-making between percutaneous coronary intervention and coronary artery bypass grafting among patients with stable multivessel and/or left main coronary artery disease.

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5.3.2 Isolated proximal left anterior descending coronary artery disease

Comparing CABG and PCI among patients with isolated proximal LAD disease, the available evidence suggests similar outcomes in terms of death, MI, and stroke, but a higher risk of repeat revascularization with PCI.[68,70,73,101,139–144]

5.3.3 Left main coronary artery disease

The available evidence from RCTs and meta-analyses comparing CABG with PCI using DES among patients with LM disease suggests equivalent results for the safety composite of death, MI, and stroke up to 5 years of follow-up.[148] A significant interaction with time is notable, providing early benefit for PCI in terms of MI and peri-interventional stroke, which is subsequently offset by a higher risk of spontaneous MI during long-term follow-up. The need for repeat revascularization is higher with PCI than with CABG.

The EXCEL trial compared CABG with PCI using new-generation DES (EES) among 1905 patients with significant LM disease.[107] At 3 years of follow-up, the primary endpoint of death, stroke, or MI occurred with similar frequency in the CABG and PCI group (14.7 vs. 15.4%; HR 1.00, 95% CI 0.79–1.26, $P = 0.98$). The pre-planned landmark analysis from 30 days to 3 years showed a significant difference for the primary endpoint in favour of CABG (7.9 vs. 11.5%, $P = 0.02$).

The NOBLE (Nordic-Baltic-British Left Main Revascularization Study) trial compared CABG with PCI using new-generation DES [biolimus-eluting stents (BES)] among 1201 patients with significant LM disease (mean SYNTAX score of 23).[106] At a median follow-up of 3.1 years, the primary endpoint of death, non-procedural MI, stroke, and repeat revascularization occurred more frequently in the PCI than the CABG group (29 vs. 19%; HR 1.48, 95% CI 1.11–1.96, $P = 0.007$).

A recent collaborative individual patient pooled analysis of randomized trials including 11 518 patients reviewed the currently available evidence from randomized trials comparing CABG with PCI for LM or multivessel disease.[124] The primary outcome was all-cause mortality. In the overall cohort, CABG was associated with a significant survival benefit during a mean follow-up of 3.8 ± 1.4 years (5 year all-cause mortality 11.2% after PCI vs. 9.2% after CABG; HR 1.20, 95% CI 1.06–1.37, $P = 0.0038$). There was a linear trend for HRs of death increasing with increasing SYNTAX tertiles [$P = 0.0011$ for trend (unpublished analysis)]. However, among 4478 patients with LM disease, those randomly assigned to CABG or PCI with a mean follow-up of 3.4 ± 1.4 years reported similar risks for the primary outcome all-cause mortality (PCI 10.7 vs. CABG 10.5%; HR 1.07, 95% CI 0.87–1.33, $P = 0.52$) at 5 years. There were no significant differences in mortality between PCI and CABG in subgroup analyses according to SYNTAX scores. Nevertheless, in patients with a high SYNTAX score, a trend towards better survival was noted with CABG. The proportion of patients with a high SYNTAX score was limited in view of the inclusion criteria of the respective studies.

Current evidence indicates that PCI is an appropriate alternative to CABG in LM disease and low-to-intermediate anatomical complexity. Among patients with LM disease and low anatomical complexity, there is evidence that the outcomes with respect to major clinical endpoints are similar for PCI and CABG, resulting in a class I recommendation. Among patients with LM disease and high anatomical complexity, the number of patients studied in RCTs is low due to exclusion criteria; the risk estimates and CIs are imprecise, but suggest a trend towards better survival with CABG. Therefore, PCI in this setting cannot be endorsed as reflected by a class III recommendation. For PCI in LM with intermediate anatomical complexity, the previous class IIa recommendation was maintained in view of the incomplete 5 year follow-up of the two largest RCTs in this setting.

5.3.4 Multivessel coronary artery disease

The observation of a survival advantage of CABG over PCI has been consistent among patients with severe three-vessel CAD (intermediate to high SYNTAX score), and has been attributed at least in part to the placement of bypass grafts to the mid coronary vessels providing prophylaxis against the development of new proximal disease.

The BEST trial, comparing CABG with PCI using new-generation DES (EES) among patients with multivessel CAD (77% three-vessel CAD and 23% two-vessel disease, mean SYNTAX score 24), prematurely stopped enrolment after the inclusion of 880 patients due to slow recruitment.[105] At a median follow-up of 4.6 years, PCI was associated with a higher incidence of the primary endpoint (death, MI, and TVR) (15.3 vs. 10.6%; HR 1.47, 95% CI 1.01–2.13, $P = 0.04$) than CABG. The risk of death, MI, and stroke was not statistically different between the two treatment groups (11.9 vs. 9.5%; HR 1.26, 95% CI 0.84–1.89, $P = 0.26$), whereas repeat revascularization of any vessel (11.0 vs. 5.4%; HR 2.1, 95% CI 1.28–3.41, $P = 0.003$) but not target lesion revascularization (5.7 vs. 3.8%; HR 1.51, 95% CI 0.82–2.80, $P = 0.19$) was more frequent in the PCI group. CABG resulted in more complete revascularization (71.5 vs. 50.9%; $P < 0.001$) and a lower incidence of revascularization for new lesions (5.5 vs. 2.3%; HR 2.47, 95% CI 1.18–5.17, $P = 0.01$).

Consistent with findings in the overall cohort (see section 5.3.3), the collaborative individual patient pooled analysis found that in 7040 patients with multivessel disease, those assigned to CABG had significantly lower 5 year all-cause mortality than those assigned to PCI (PCI 11.5 vs. CABG 8.9%; HR 1.28, 95% CI 1.09–1.49, $P = 0.0019$).[124] Outcomes for the endpoint all-cause mortality were modified by two variables, diabetes and disease complexity, as assessed by the SYNTAX score. Compared with patients without diabetes (8.7 vs. 8.0%; HR 1.08, 95% CI 0.86–1.36, $P = 0.49$), mortality was higher after PCI than CABG in patients with diabetes (15.5 vs. 10.0%; HR 1.48, 95% CI 1.19–1.84, $P = 0.0004$, $P_{interaction} = 0.045$). There was a gradient of risk with a stepwise increase in mortality for PCI according to SYNTAX score tertile (SYNTAX score 0 - 22: 10.5 vs. 8.4%; HR 1.11, 95% CI 0.77–1.62, $P = 0.57$; SYNTAX score 23 - 32: 14.0 vs. 9.5%; HR 1.50, 95% CI 1.09–2.08, $P = 0.0129$; SYNTAX score >32: 19.2 vs. 11.2%; HR 1.70, 95% CI 1.13–2.55, $P = 0.0094$).

An individual patient data pooled analysis of SYNTAX and BEST, comparing CABG with PCI using DES among 1275 patients with multivessel disease in the absence of diabetes (89% three-vessel CAD, mean SYNTAX score 26), reported a lower risk of death (6.0 vs. 9.3%; HR 0.65, 95% CI 0.43–0.98, $P = 0.04$) and MI (3.3 vs. 8.3%; HR 0.40, 95% CI 0.24–0.65, $P < 0.001$) in the CABG group at a median follow-up of 61 months.[149] The risk of death was not significantly different among patients with a low (0 - 22) SYNTAX score (6.0 vs. 7.5%, $P = 0.66$), whereas the benefit of CABG over PCI was greater in patients with an intermediate-to-high (>22) SYNTAX score (7.1

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vs. 11.6%, $P = 0.02$). Another individual patient data pooled analysis of SYNTAX and BEST, comparing CABG with PCI using DES among 1166 patients with multivessel disease involving the proximal LAD (88% three-vessel CAD, mean SYNTAX score 28), reported a higher risk of the composite of death, MI, and stroke (16.3 vs. 11.5%; HR 1.43, 95% CI 1.05–1.96, $P = 0.02$), cardiac death, MI, and repeat revascularization in the PCI group at 5 years of follow-up.[147] Of note, outcomes were not significantly different for CABG and PCI for any endpoint except for MI among the subgroup of patients with low SYNTAX score (0 - 22).

The available evidence suggests that in multivessel CAD without diabetes and low anatomical complexity, PCI and CABG achieve similar long-term outcomes with respect to survival and the composite of death, MI, and stroke, justifying a class I recommendation for PCI. In patients with multivessel CAD and intermediate-to-high anatomical complexity, the two large trials using DES, SYNTAX and BEST, found a significantly higher mortality and a higher incidence of death, MI, and stroke with PCI in the absence of diabetes. Consistent results were also obtained for patients with multivessel CAD in the recent individual patient-level meta-analysis.[124] Thus, the previous class III recommendation for PCI in multivessel CAD and intermediate-to-high complexity was maintained.

5.4 Gaps in the evidence

It remains to be determined whether revascularization by PCI improves prognosis in patients with SCAD. The ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) study (NCT01471522) is currently recruiting 5000 patients with SCAD and evidence of moderate-to-severe ischaemia detected by non-invasive imaging, who are randomized before coronary angiography to medical therapy or an invasive strategy to detect differences in the primary endpoint of death or MI. Current techniques rely on coronary angiography and the detection of ischaemia-producing lesions. However, future adverse events are related at least in part to non-flow limiting, vulnerable plaques. Better identification of vulnerable plaques and the development of appropriate treatment strategies is needed. Along the same lines, the completeness and timing of revascularization are not well defined, and neither are the roles of residual ischaemia and lesions. Moreover, we need more research on the use of the SYNTAX and other scores for informing treatment allocation, as well as dedicated trials in specific subsets. Very long-term, extended follow-up (10 years) of trials comparing PCI and CABG, particularly in the setting of LM disease, will provide further insights into the relative merits of both revascularization techniques.

6 Revascularization in non-ST-elevation acute coronary syndrome

Myocardial revascularization in patients with non-ST-segment elevation ACS (NSTE-ACS) is addressed by prior Guidelines that are endorsed by the current Task Force.[158] In the present Guidelines, we discuss new evidence where previous recommendations require an update.

6.1 Early invasive vs. conservative strategy

An invasive strategy has become the standard of care for high-risk patients.[158] This approach allows prompt diagnosis of the underlying CAD, identification of the culprit lesion, guidance for antithrombotic management, and the assessment of the suitability of coronary anatomy for PCI or CABG. Numerous factors interplay in the decision-making process, including clinical presentation, comorbidities, risk stratification (*Figure 4*), and high-risk features specific for a revascularization modality such as frailty, cognitive status, estimated life expectancy, and the functional and anatomical severity of CAD.

Up to 40% of NSTE-ACS patients with obstructive CAD present with multiple complex plaques[159–162] and 25% with an acute occluded coronary artery,[163] so that identification of the culprit lesion may be challenging. Correlation with ECG or echo changes and the use of OCT in the 25% of NSTE-ACS patients with angiographically normal epicardial coronary arteries[164–166] may be helpful for identifying the culprit lesion, or rule out other mechanisms such as dissection or haematomas [MI with non-obstructive coronary arteries (MINOCA)].[167–169]

A routine invasive strategy in NSTE-ACS has been shown to improve clinical outcomes,[170] and benefit was mainly confined to biomarker-positive patients[171] and patients with other high-risk features as defined in *Figure 4*. Of importance, the use of a radial approach, new-generation DES, and more effective $P2Y_{12}$-inhibitors were not available or broadly implemented in these trials, and led to a magnified benefit in frail ACS populations.[172,173]

6.2 Timing of angiography and intervention

The current recommendations on the timing of angiography and intervention, as defined in *Figure 4*, are based on evidence discussed in detail by the prior Guidelines on NSTE-ACS.[158] Specifically, a reduction in recurrent or refractory ischaemia and length of hospital stay was found with early intervention.[174,175] More recently, an updated collaborative meta-analysis on individual published and unpublished data ($n = 5324$ patients with a median follow-up of 180 days) suggested that early intervention might also be associated with decreased mortality.[176] This meta-analysis showed a statistical trend towards decreased mortality with an early invasive strategy compared with a delayed invasive strategy in unselected patients with NSTE-ACS (HR 0.81, 95% CI 0.64–1.03, $P = 0.088$). The survival benefit of the early invasive strategy appeared more pronounced in high-risk subsets, including elevated cardiac biomarkers at baseline (HR 0.76, 95% CI 0.58–0.996), diabetes (HR 0.67, 95% CI 0.45–0.99), a Global Registry of Acute Coronary Events risk score >140 (HR 0.70, 95% CI 0.52–0.95), and age 75 years or older (HR 0.65, 95% CI 0.46–0.93), although tests for interaction were inconclusive.

6.3 Type of revascularization

6.3.1 Percutaneous coronary intervention

6.3.1.1 Technical aspects

Implantation of new-generation DES is the standard treatment strategy even when dual antiplatelet therapy (DAPT) cannot be sustained beyond 1 month post-intervention[173,177–179] (see section 17), and the radial approach has also become the standard of care.[172]

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DAPT is recommended for 12 months irrespective of stent type, while in patients at high ischaemic risk not experiencing bleeding events, DAPT may be extended (see section 17). There is no evidence for any additional benefit of thrombectomy in patients undergoing PCI in the setting of NSTE-ACS.[180] While FFR is considered the invasive gold standard for the functional assessment of lesion severity in SCAD, it has been shown to be feasible, reliable, safe, and effective in NSTE-ACS patients with multivessel disease, although its prognostic value is unclear.[22,137,181]

6.3.1.2 Revascularization strategies and outcomes

Complete revascularization of significant lesions should be attempted in multivessel disease NSTE-ACS patients, given that it was mandated in trials testing early vs. late intervention[171,182,183] and that the prognosis of patients with incomplete revascularization is known to be worse.[131,184] In addition, it seems that complete one-stage revascularization is associated with better clinical outcome than multistage PCI.[185] The risk of periprocedural complications of PCI defined as MI or myocardial injury, as well as that of long-term ischaemia, remains higher in NSTE-ACS than in stable patients.[186,187] For ACS patients who have undergone PCI, revascularization procedures represent the most frequent, most costly, and earliest causes for rehospitalization.[188,189] As in ST-elevation myocardial infarction (STEMI), routine treatment of non-culprit lesions during the primary intervention by PCI is harmful in NSTE-ACS patients with cardiogenic shock, as shown by the recently published CULPRIT-SHOCK (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock) trial (see section 7.3).[190]

6.3.2 Coronary artery bypass grafting

Approximately 5–10% of NSTE-ACS patients require CABG,[191] and they represent a challenging subgroup given their high-risk characteristics compared with patients undergoing elective CABG.[192] In the absence of randomized data, optimal timing for non-emergent CABG in NSTE-ACS patients should be determined individually. The risk of ischaemic events possibly related to suboptimal antiplatelet therapy while awaiting surgery is <0.1%, while that of perioperative bleeding complications associated with platelet inhibitors is >10%.[193] In patients with ongoing ischaemia or haemodynamic instability with an indication for CABG, emergency surgery should be performed and not postponed as a consequence of antiplatelet treatment exposure.

6.3.3 Percutaneous coronary intervention vs. coronary artery bypass grafting

There is no randomized comparison of PCI vs. CABG in the specific setting of NSTE-ACS. The currently available evidence indirectly suggests that the criteria applied to patients with SCAD to guide the choice of revascularization modality should be applied to stabilized patients with NSTE-ACS.[100,121,150,194] Recent individual-patients data analysis from the BEST, PRECOMBAT, and SYNTAX studies compared the outcome of CABG with that of PCI in 1246 patients with stabilized NSTE-ACS and multivessel or LM disease.[194] The 5 year incidence of the primary outcome—the composite of death, MI, or stroke—was significantly lower with CABG than with PCI (13.4 vs. 18%, $P = 0.036$). The findings of this meta-analysis were consistent with the main findings of the studies included, thus supporting the concept that the principles of SCAD should apply to stabilized patients with NSTE-ACS as well.

For complex cases, Heart Team discussion and use of the SYNTAX score are recommended,[195] given its ability to predict death, MI, and revascularization in patients with NSTE-ACS and multivessel disease undergoing PCI. In patients with multivessel disease and diabetes in particular, recent evidence suggests a greater benefit of CABG vs. PCI.[196]

Recommendations for invasive evaluation and revascularization in non-ST-elevation acute coronary syndrome

Recommendations	Class[a]	Level[b]
Urgent coronary angiography (<2 h) is recommended in patients at very high ischaemic risk (*Figure 4*).[197]	I	C
An early invasive strategy (<24 h) is recommended in patients with at least one high-risk criterion (*Figure 4*).[164,174,176]	I	A
An invasive strategy (<72 h after first presentation) is indicated in patients with at least one intermediate-risk criterion (*Figure 4*) or recurrent symptoms.[170,171]	I	A
It is recommended to base the revascularization strategy (*ad hoc* culprit lesion PCI/multivessel PCI/CABG) on the clinical status and comorbidities, as well as the disease severity [i.e. the distribution and angiographic lesion characteristics (e.g. SYNTAX score)], according to the principles for SCAD.[c] [194]	I	B
In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended during primary PCI.[190]	III	B

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CABG = coronary artery bypass grafting; IRA = infarct-related artery; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; SYNTAX = Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.
[a]Class of recommendation.
[b]Level of evidence.
[c]May apply to stabilized NSTE-ACS patients.

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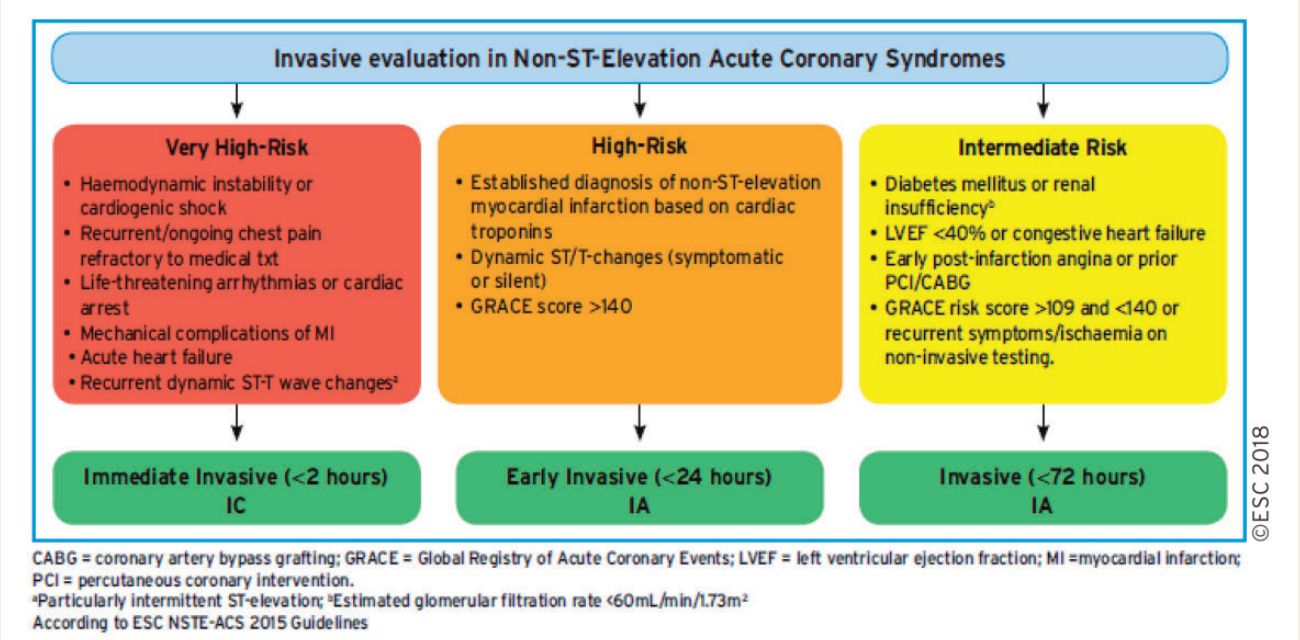

CABG = coronary artery bypass grafting; GRACE = Global Registry of Acute Coronary Events; LVEF = left ventricular ejection fraction; MI =myocardial infarction; PCI = percutaneous coronary intervention.
[a]Particularly intermittent ST-elevation; [b]Estimated glomerular filtration rate <60mL/min/1.73m²
According to ESC NSTE-ACS 2015 Guidelines

Figure 4 Selection of non-ST-elevation acute coronary syndrome treatment strategy and timing according to initial risk stratification.

6.4 Gaps in the evidence

In the setting of NSTE-ACS, there are no dedicated prospective studies on the revascularization strategy with multivessel disease. Thus, current recommendations on the choice of lesions to be treated and treatment modality (PCI or CABG) are based on an analogy to findings obtained in SCAD or STEMI. Likewise, the prognostic role of FFR and iwFR in guiding myocardial revascularization needs additional clarification.

7 Revascularization in ST-segment elevation myocardial infarction

Myocardial revascularization in patients with STEMI is addressed by the 2017 ESC Guidelines on STEMI. After reviewing the subsequent literature, the current Task Force endorses most recommendations of these Guidelines.[198]

7.1 Time delays

Delays in the timely implementation of reperfusion therapy are key issues in the management of STEMI. Detailed recommendations on timelines, logistics, and pre-hospital management have been provided in the recent ESC STEMI Guidelines (*Figure 5*).[198]

A recent analysis of 12 675 STEMI patients in the FITT-STEMI (Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction) trial emphasizes the strong impact of time delays on mortality, particularly in STEMI patients with cardiogenic shock or out-of-hospital cardiac arrest.[199] In shock without out-of-hospital cardiac arrest, every 10 min treatment delay between 60–180 min from the first medical contact resulted in 3.3 additional deaths per 100 PCI-treated patients, and in 1.3 additional deaths after out-of-hospital cardiac arrest without cardiogenic shock. In stable STEMI patients, time delays were substantially less relevant (0.3 additional deaths per 100 PCI-treated patients for every 10 min delay between 60–180 min from the first medical contact). Thus, high-risk STEMI patients with cardiogenic shock or out-of-hospital cardiac arrest are those who benefit most from expediting all steps of the care pathway.

7.2 Selection of reperfusion strategy

Primary PCI, defined as percutaneous catheter intervention in the setting of STEMI without previous fibrinolysis, is the preferred reperfusion strategy. It has replaced fibrinolysis in patients with STEMI, provided it can be performed in a timely manner in high-volume PCI centres with experienced operators and 24 h/7 days a week catheterization laboratory activation.[198,200,201] In settings where primary PCI cannot be performed in a timely fashion, fibrinolysis should be administered as soon as possible. If first medical contact (FMC) is out-of-hospital, lysis should be implemented pre-hospital (e.g. in the ambulance) (*Figure 5*).[202–206] It should be followed by transfer to PCI-capable centres for routine coronary angiography in all patients, and should be performed without delay for rescue PCI in the case of unsuccessful fibrinolysis or within 2–24 h after bolus administration.[198] Emergency CABG may be indicated in selected STEMI patients unsuitable for PCI.

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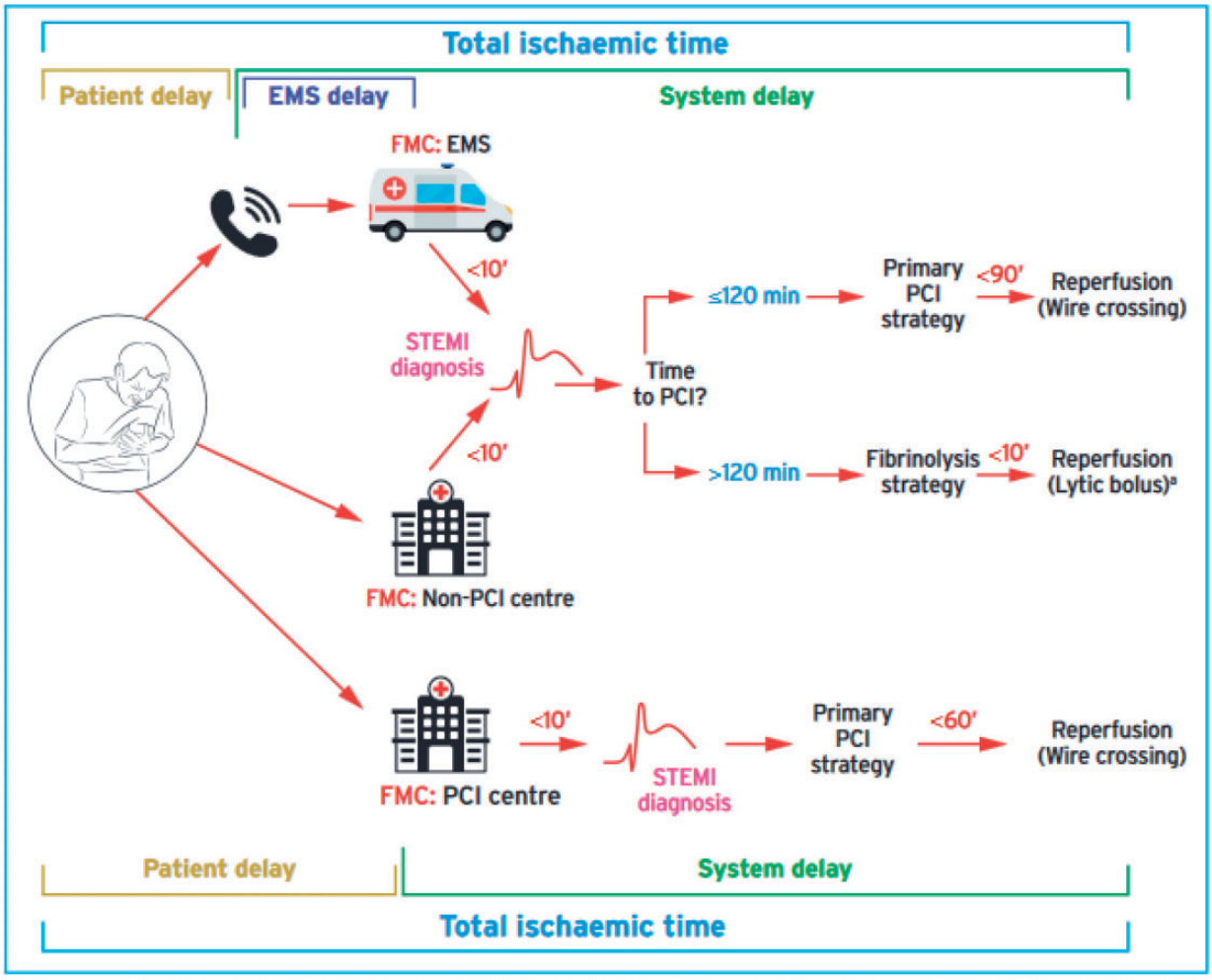

The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the choice of reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when the EMS arrives at the scene. EMS = emergency medical service.
FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction. 'denotes minutes.
[a]Patients receiving fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.

Figure 5 Modes of patient's medical contact, components of ischaemia time, and flowchart for reperfusion strategy selection.

7.3 Primary percutaneous coronary intervention

Key points for optimizing and guiding primary PCI are summarized below.

The infarct-related artery (IRA) should be systematically treated during the initial intervention. Patients with extensive CAD in vessels remote from the IRA have an adverse prognosis following primary PCI.[207] Staged PCI in patients with multivessel disease and no haemodynamic compromise is an independent predictor of survival, and more frequent ischaemic events have been reported in direct vs. staged revascularization of STEMI patients with multivessel disease.[208–210]

Four major randomized trials-PRAMI (Preventive Angioplasty in Acute Myocardial Infarction),[211] CvLPRIT (Complete Versus Lesion-Only Primary PCI trial),[212] DANAMI-3-PRIMULTI (The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: PRImary PCI in MULTIvessel Disease),[213] and Compare-Acute[214]-have consistently shown a benefit of complete revascularization (performed immediately or staged) as compared with IRA-only PCI in patients with STEMI and multivessel disease (for details see the Supplementary Data). A recent meta-analysis of 10 trials has shown that complete revascularization was associated with a lower risk of MACE (RR 0.57, 95% CI 0.42–0.77), due to a lower risk of urgent revascularization

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(RR 0.44, 95% CI 0.30–0.66), with no significant difference in mortality (RR 0.76, 95% CI 0.52–1.12) or MI (RR 0.54, 95% CI 0.23–1.27).[215] This meta-analysis did not include Compare-Acute. Yet, similar to earlier studies, the benefit of complete revascularization over culprit-only revascularization seen in Compare-Acute was driven by a lower need for unplanned reintervention, whereas the incidences of death and recurrent MI were similar between the two strategies.[214]

Most of the studies support the concept of full revascularization either during the initial hospital stay for STEMI or a staged admission,[215] but it remains to be determined how clinicians can identify lesions that should be revascularized beyond the culprit lesion and whether complete revascularization should be performed in single- or multi-stage procedures. Moreover, there is a lack of evidence on the optimal timing of staged procedures. In most of the studies, staged procedures were performed during the initial hospital stay. At present, one-stage multivessel PCI during STEMI without cardiogenic shock should be considered in patients in the presence of multiple, critical stenoses or highly unstable lesions (angiographic signs of possible thrombus or lesion disruption), and if there is persistent ischaemia after PCI on the supposed culprit lesion.

In patients with multivessel disease and AMI with cardiogenic shock, the recently published CULPRIT-SHOCK trial showed that a strategy with PCI of the culprit lesion only with possible staged revascularization determined a lower 30 day risk of the composite of all-cause mortality or severe renal failure compared with immediate multivessel PCI.[190] This was driven by a significant risk reduction in 30 day all-cause mortality by the culprit lesion-only strategy compared with immediate multivessel PCI (43.3 vs. 51.6%; HR 0.84, 95% CI 0.72–0.98, $P = 0.03$). These findings need to be interpreted in light of a low 12.5% (43 out of 344 patients) crossover rate from culprit lesion-only to immediate multivessel PCI based on physicians' judgment. Based on these findings, culprit lesion-only PCI is recommended as the default strategy in patients with AMI with cardiogenic shock. A more detailed discussion of the revascularization strategy in MI patients with cardiogenic shock is found in the Supplementary Data.

In patients with STEMI, DES (in particular new-generation DES) have demonstrated better efficacy as compared with BMS and should be used as the default strategy in STEMI patients, even when DAPT cannot be sustained beyond 1 month.[177,178,216–218] (see section 16.1.2). As discussed in section 16.4, radial access is preferred over femoral access.

Delaying stenting in primary PCI has been investigated as an option to reduce microvascular obstruction (MVO) and preserve microcirculatory function in two small trials with conflicting results.[219,220] More recently, in the larger deferred vs. conventional stent implantation in patients with STEMI [The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: DEFERred stent implantation in connection with primary PCI (DANAMI 3-DEFER)] trial in 1215 STEMI patients, there was no effect on the primary clinical outcome (composite of death, non-fatal MI, or ischaemia-driven revascularization of non-IRA lesions) over a median follow-up of 42 months.[221] Routine deferred stenting was associated with a higher risk of TVR.

Thrombus aspiration has been proposed as an adjunct during primary PCI to further improve epicardial and myocardial reperfusion by the prevention of distal embolization of thrombotic material and plaque debris.[222] Two landmark RCTs, which were adequately powered to detect the superiority of routine manual thrombus aspiration vs. conventional PCI, showed no benefit on clinical outcomes of the routine aspiration strategy overall or in any subgroup of patients indicating high thrombotic risk.[223–226] A safety concern emerged in TOTAL (Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI) trial with an increase in the risk of stroke.[225,227] Taken together, these results suggest that the routine use of thrombus aspiration is not indicated. In the high-thrombus burden subgroup, the trend towards reduced cardiovascular death and increased stroke/transient ischaemic attack (TIA) provides a rationale for future trials of improved thrombus aspiration technologies in this high-risk subgroup (although statistical tests did not support significant subgroup interaction).[228]

7.4 Percutaneous coronary intervention after thrombolysis and in patients with late diagnosis

The benefits of early, routine PCI after thrombolysis were seen in the absence of an increased risk of adverse events (stroke or major bleeding). Based on data from the four most recent trials, all of which had a median delay between the start of thrombolysis and angiography of 2–6 h, a time frame of 2–24 h after successful lysis is recommended.[206,229–231] In cases of failed fibrinolysis, or if there is evidence of re-occlusion or reinfarction with recurrence of ST-segment elevation, the patient should undergo immediate coronary angiography and rescue PCI.[232] Patients presenting between 12 and 48 h after the onset of symptoms, even if pain free and with stable haemodynamics, may still benefit from early coronary angiography and possibly PCI.[233,234] In patients presenting days after the acute event with a completed MI, only those with recurrent angina or documented residual ischaemia—and proven viability on non-invasive imaging in a large myocardial territory—may be considered for revascularization when the infarct artery is occluded. Routine late PCI of an occluded IRA after MI in stable patients has no incremental benefit over medical therapy.[235]

7.5 Gaps in the evidence

Patients undergoing primary PCI benefit from full revascularization, but the optimal timing of treatment of the non-culprit lesion is not known. More studies evaluating the assessment of non-culprit lesions by FFR or iwFR at the time of acute PCI, and studies investigating whether intravascular imaging guidance of primary PCI can improve the outcomes of STEMI patients, are needed. Future trials of improved thrombus aspiration technologies may address the role of this strategy in patients with high-risk features, such as large thrombus burden.[228]

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Primary percutaneous coronary intervention for myocardial reperfusion in ST-elevation myocardial infarction: indications and logistics

Recommendations	Class[a]	Level[b]
Indication		
Reperfusion therapy is indicated in all patients with time from symptom onset <12 h duration and persistent ST-segment elevation.[200,201,236]	I	A
In the absence of ST-segment elevation, a primary PCI strategy is indicated in patients with suspected ongoing ischaemic symptoms suggestive of MI and at least one of the following criteria present: • haemodynamic instability or cardiogenic shock • recurrent or ongoing chest pain refractory to medical treatment • life-threatening arrhythmias or cardiac arrest • mechanical complications of MI • acute heart failure • recurrent dynamic ST-segment or T-wave changes, particularly with intermittent ST-segment elevation.	I	C
A primary PCI strategy is recommended over fibrinolysis within the indicated time frames.[200,201,237,238]	I	A
In patients with time from symptom onset >12 h, a primary PCI strategy is indicated in the presence of ongoing symptoms or signs suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias.	I	C
A routine primary PCI strategy should be considered in patients presenting late (12–48 h) after symptom onset.[233,234,239]	IIa	B
Logistics		
It is recommended that the pre-hospital management of STEMI patients should be based on regional networks that are designed to deliver reperfusion therapy effectively in a timely fashion, and to offer primary PCI to as many patients as possible.[240,241]	I	B
It is recommended that all EMS, emergency departments, coronary care units, and catheterization laboratories have a written updated STEMI management protocol, preferably shared within geographical networks.	I	C
It is recommended that primary PCI-capable centres deliver a 24 h/7 day service and ensure that primary PCI is performed as fast as possible.[242–244]	I	B
It is recommended that patients transferred to a PCI-capable centre for primary PCI bypass the emergency department and CCU/ICCU, and are transferred directly to the catheterization laboratory.[245–247]	I	B

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CCU = coronary care unit; EMS = emergency medical services; ICCU = intensive coronary care unit; MI = myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence.

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Primary percutaneous coronary intervention for myocardial reperfusion in ST-elevation myocardial infarction: procedural aspects (strategy and technique)

Recommendations	Class[a]	Level[b]
Strategy		
Routine revascularization of non-IRA lesions should be considered in patients with multivessel disease before hospital discharge.[211–214]	IIa	A
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardized myocardium if PCI of the IRA cannot be performed.	IIa	C
In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended during primary PCI.[190]	III	B
Technique		
Routine use of thrombus aspiration is not recommended.[223–226,228]	III	A

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CABG = coronary artery bypass grafting; IRA = infarct-related artery; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence.

8 Myocardial revascularization in patients with heart failure

8.1 Chronic heart failure

8.1.1 Recommendations for myocardial revascularization in patients with chronic heart failure

When compared with medical therapy alone, coronary revascularization is superior in improving survival in patients with HF of ischaemic origin and is recommended in clinical practice.[81,248] However, the optimal revascularization strategy is not defined. The choice between CABG and PCI should be made by the Heart Team after careful evaluation of the patient's clinical status and coronary anatomy, expected completeness of revascularization (see section 5.3.1.3), myocardial viability, coexisting valvular disease, and comorbidities. Considerations relating to the need for viability testing prior to revascularization are discussed in section 3.

Randomized clinical trial data comparing revascularization with medical therapy exists only for CABG in the setting of the STICH trial.[81] One analysis from this trial showed that CABG can be performed with acceptable 30 day mortality rates (5.1%) in patients with LV dysfunction (LVEF ≤35%).[249] Extended follow-up in the STICH Extension Study (STICHES) supports a significant survival benefit of CABG combined with medical therapy vs. medical therapy alone in a 10 year observation period.[81]

There are currently no dedicated randomized clinical trials comparing PCI vs. medical therapy in patients with HF with reduced EF (HFrEF). In addition, CABG vs. PCI randomized trials have excluded patients with severe HF. In one prospective registry including 4616 patients with multivessel disease and severe HFrEF, propensity score-matched comparison revealed similar survival (mean follow-up 2.9 years) with PCI (using EES) vs. CABG.[250] PCI was associated with a higher risk of MI, particularly in patients with incomplete revascularization, and repeat revascularization. CABG was associated with a higher risk of stroke. The conclusion of the study was that multivessel PCI can be a valuable option in HF patients if complete revascularization is possible. A systematic review of studies comparing revascularization with medical therapy in patients with an EF ≤40% showed that there was a significant mortality reduction with CABG (HR 0.66, 95% CI 0.61–0.72, P <0.001) and PCI (HR 0.73, 95% CI 0.62–0.85, P <0.001) vs. medical therapy, though these finding are limited by the predominantly observational nature of the included studies and missing information on the completeness of revascularization.[248]

A recent observational study investigated outcomes with PCI or CABG for multivessel CAD and LV dysfunction in 1738 propensity-matched patients with diabetes mellitus.[251] Similar to the findings in the absence of LV dysfunction, when CABG was compared with PCI it was associated with a significantly lower risk of MACE, which included a significant reduction in mortality. Event curves separated early during the first year and continued to separate out to 12 years.

PCI should be considered in older patients without diabetes in whom complete revascularization can be achieved, whereas CABG is preferred in younger patients with more extensive CAD or those with diabetes. In patients with diabetes and LV moderate or severe dysfunction (EF <50%), CABG is associated with better long-term survival and reduced incidence of MACCE.[250,251]

8.1.2 Ventricular reconstruction and aneurysm resection

The aim of surgical ventricular reconstruction (SVR) is to restore physiological volume, and achieve an elliptical shape of the LV, by scar resection and LV wall reconstruction on a mannequin of predefined size. The aim of ventricular aneurysmectomy is to remove fibrous scars in cases of severe dilatation, thrombus formation, or as a source of life-threatening ventricular arrhythmias.

The STICH trial revealed no difference in the primary outcome (total mortality or cardiac hospitalization) between patients randomly allocated to CABG vs. combined CABG and SVR.[252] Subgroup analyses of patients with a less dilated LV and better LVEF showed benefit from SVR.[253] In the STICH trial, a post-operative LV end-systolic volume index ≤70 mL/m^2, after CABG plus SVR, resulted in improved survival compared with CABG alone.[252,254] In experienced centres, SVR may be done at the time of CABG if HF

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symptoms are more predominant than angina, and if myocardial scar and moderate LV remodelling are present.

Recommendations on revascularizations in patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction ≤35%)

Recommendations	Class[a]	Level[b]
In patients with severe LV systolic dysfunction and coronary artery disease suitable for intervention, myocardial revascularization is recommended.[81,250]	I	B
CABG is recommended as the first revascularization strategy choice in patients with multivessel disease and acceptable surgical risk.[68,81,248,255]	I	B
In patients with one- or two-vessel disease, PCI should be considered as an alternative to CABG when complete revascularization can be achieved.	IIa	C
In patients with three-vessel disease, PCI should be considered based on the evaluation by the Heart Team of the patient's coronary anatomy, the expected completeness of revascularization, diabetes status, and comorbidities.	IIa	C
LV aneurysmectomy during CABG should be considered in patients with NYHA class III/IV, large LV aneurysm, large thrombus formation, or if the aneurysm is the origin of arrhythmias.	IIa	C
Surgical ventricular restoration during CABG may be considered in selected patients treated in centres with expertise.[252–254,256,257]	IIb	B

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CABG = coronary artery bypass grafting; LV = left ventricular; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

8.2 Acute heart failure and cardiogenic shock

Acute myocardial ischaemia in the setting of AMI is the antecedent event for the majority of patients with cardiogenic shock undergoing percutaneous revascularization. Mechanical complications—such as papillary muscle rupture with severe mitral valve regurgitation, ventricular septal defect, or free wall rupture—are additional precipitating causes.

8.2.1 Revascularization

The SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial demonstrated that in patients with cardiogenic shock complicating AMI, emergency revascularization with PCI or CABG improved long-term survival when compared with initial intensive medical therapy. All-cause mortality at 6 months was lower in the group assigned to revascularization than in the medically treated patients (50.3 vs. 63.1%, respectively; RR 0.80, 95% CI 0.65–0.98, $P = 0.03$).[258]

The revascularization strategy for patients with cardiogenic shock and multivessel disease is addressed in section 7.

A subanalysis of the SHOCK trial comparing patients treated with CABG or PCI showed similar survival rates between the two subgroups.[259] There were more patients with diabetes (48.9 vs. 26.9%; $P = 0.02$), three-vessel disease (80.4 vs. 60.3%; $P = 0.03$), and LM coronary disease (41.3 vs. 13.0%; $P = 0.001$) in the CABG group. The findings of this non-randomized comparison suggest that CABG should be considered in patients with cardiogenic shock who have suitable anatomy, particularly if successful PCI is not feasible.

8.2.2 Mechanical circulatory support

Short-term MCS devices that are currently available are the intra-aortic balloon pump (IABP), veno-arterial extracorporeal membrane oxygenation (ECMO), and percutaneous left ventricular assist devices (pLVADs). Short-term MCS may be considered in refractory cardiogenic shock depending on patient age, comorbidities, neurological function, and the prospects for long-term survival and quality of life.

8.2.2.1 Intra-aortic balloon pump

IABPs are low-cost devices that are easy to insert and remove. They moderately increase cardiac output and coronary and cerebral perfusion, while decreasing ventricular workload. In patients with cardiogenic shock complicating acute MI, the IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) randomized trial (600 patients) showed that the use of IABPs did not reduce 30 day mortality and that there was no evidence of long-term benefit.[260,261] A recent Cochrane review of seven trials (790 patients) showed that IABPs may have a beneficial effect on some haemodynamic parameters but did not result in survival benefits.[262] Thus, the routine use of IABPs in patients with cardiogenic shock complicating acute MI is not recommended.

8.2.2.2 Extracorporeal membrane oxygenation

Veno-arterial ECMO (VA-ECMO), also known as extracorporeal life support (ECLS), in its current form is a modified form of cardiopulmonary bypass. It decompresses the venous system; increases coronary, cerebral, and peripheral perfusion; and also provides supplementary blood oxygenation. When performed percutaneously, it does not allow for LV decompression and leads to increasing LV afterload.

In patients with cardiac arrest, evidence from observational trials supports better survival in patients treated with VA-ECMO compared with those without.[263] When compared with IABP, VA-ECMO provides superior circulatory support.[264,265] Moreover, a meta-analysis of observational studies suggested that in patients with cardiogenic shock post-ACS, VA-ECMO showed a 33% higher 30 day survival compared with IABP [95% CI 14–52%, $P < 0.001$; number needed to treat (NNT) 13].[263] However, the low number of patients included in the analysed studies and the non-random treatment allocation are important limitations.

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8.2.2.3 Percutaneous left ventricular assist devices

The majority of clinical experience with currently available pLVADs is limited to two types of device: (i) a transaortic microaxial pump (Impella) that directly unloads the LV providing 2.5 - 5 L/min blood flow and (ii) a transseptal centrifugal assist device (TandemHeart) that unloads the LV via a cannula introduced into the left atrium through a transseptal puncture.

A recent meta-analysis on MCS in cardiogenic shock included four randomized trials investigating the efficacy and safety of pLVADs vs. IABP, and demonstrated similar short-term mortality despite initial beneficial effects on arterial blood pressure and peripheral perfusion, measured by serum lactate levels.[266] In all trials, a higher rate of bleeding from vascular access sites and a significantly higher incidence of limb ischaemia following pLVAD was noted. Similar outcomes were noted in an RCT of high-risk PCI in patients with impaired LV function. The 30 day incidence of major adverse events was not different for patients with pLVAD vs. IABP.[267]

In summary, the evidence for pLVAD is insufficient to provide a recommendation on its clinical use in cardiogenic shock.

8.2.2.4 Surgically implanted left ventricular assist devices

There are limited data on surgically-implanted LV assist device (LVAD) therapy in patients with AMI and cardiogenic shock. One multicentre registry showed that despite being more critically ill prior to implantation, patients with acute MI managed with LVAD had outcomes similar to other LVAD populations.[268]

A suggested algorithm for the management of patients with cardiogenic shock is shown in *Figure 6*.

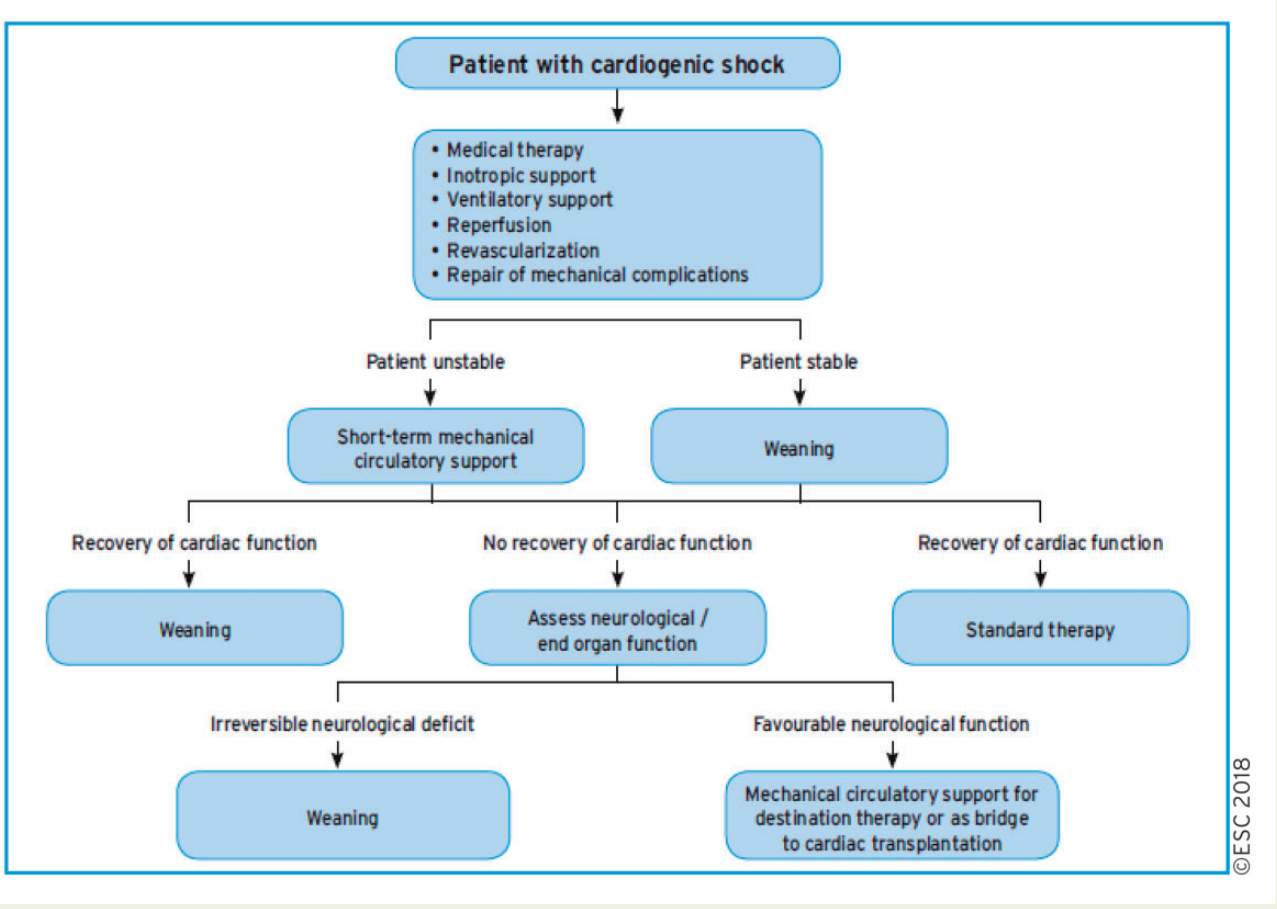

Figure 6 Algorithm for the management of patients with cardiogenic shock.

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8.3 Gaps in the evidence

There is no RCT comparing revascularization with PCI vs. CABG in patients with HF.

There is limited evidence on the role of active MCS in patients with cardiogenic shock compared with standard therapy.

Recommendations for the management of patients with cardiogenic shock

Recommendations	Class[a]	Level[b]
Emergency coronary angiography is indicated in patients with acute heart failure or cardiogenic shock complicating ACS.[258,269]	I	B
Emergency PCI of the culprit lesion is indicated for patients with cardiogenic shock due to STEMI or NSTE-ACS, independent of time delay of symptom onset, if coronary anatomy is amenable to PCI.[258]	I	B
Emergency CABG is recommended for patients with cardiogenic shock if the coronary anatomy is not amenable to PCI.[258]	I	B
In cases of haemodynamic instability, emergency surgical or catheter-based repair of mechanical complications of ACS is indicated, as decided by the Heart Team.	I	C
In selected patients with ACS and cardiogenic shock, short-term mechanical circulatory support may be considered, depending on patient age, comorbidities, neurological function, and the prospects for long-term survival and predicted quality of life.	IIb	C
Routine use of IABPs in patients with cardiogenic shock due to ACS is not recommended.[260–262]	III	B

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ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; IABP = intra-aortic balloon pump; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence

9 Revascularization in patients with diabetes

Patients with diabetes mellitus have a higher prevalence of CAD, which often manifests earlier in life and confers a substantially worse prognosis than for patients without diabetes.[270] Patients with diabetes who have suffered an MI have a worse prognosis, particularly those requiring treatment with insulin, and the presence of diabetes amplifies the risk of any cardiovascular event.[271] Diabetes mellitus is present in 25–30% of patients admitted with ACS and in up to 40% of patients undergoing CABG.[272]

The anatomical pattern of CAD in patients with diabetes clearly influences their prognosis and response to revascularization. Angiographic studies have demonstrated that patients with diabetes are more likely to have LM disease and multivessel CAD, with more diffuse disease involving smaller vessels.[273] In addition, patients with diabetes have a greater atherosclerotic burden and an increased number of lipid-rich plaques, which are prone to rupture,[274,275] and those with unstable angina have more fissured plaques and intracoronary thrombi.[276] Patients with diabetes undergoing revascularization, either with CABG or PCI, are at greater risk of kidney injury than patients without diabetes.

9.1 Evidence for myocardial revascularization

In patients with diabetes, the indications for myocardial revascularization are the same as those in patients without diabetes (see sections 5, 6, and 7). A meta-analysis of nine RCTs with 9904 ACS patients did not show an interaction between diabetic status and the benefit from invasive management and revascularization.[277] Yet, absolute risk reductions were larger in the diabetic subsets compared with non-diabetic subsets. Consistent with the findings in the absence of diabetes, the adverse impact of incomplete revascularization in patients with diabetes was also demonstrated in the BARI-2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial.[278]

Data from randomized trials on revascularization in patients with diabetes are summarized in Supplementary *Table 5*.

9.2 Type of myocardial revascularization

The selection of the optimal myocardial revascularization strategy for patients with diabetes and multivessel CAD requires particular consideration. The recommendations are provided in section 5.

9.2.1. Randomized clinical trials

The FREEDOM trial compared elective revascularization with CABG or PCI with first-generation DES (94%) in 1900 patients with diabetes (6% of the screened population) with multivessel disease but without LM stenosis.[150] The primary endpoint of any-cause death, non-fatal MI, or stroke at 5 years occurred in 26.6% in the PCI group, compared with 18.7% in the CABG group (absolute difference 7.9%, 95% CI 3.3–12.5%, $P = 0.005$). The incidences of death (16.3% in the PCI group vs. 10.9% in the CABG group; absolute difference 5.4%, 95% CI 1.5–9.2%, $P = 0.049$) and MI (13.9% in the PCI group vs. 6.0% in the CABG group, $P < 0.001$) were higher in the PCI group, but the incidence of stroke was lower (2.4 vs. 5.2%; $P = 0.03$). Within the FREEDOM trial at 5 years, patients with diabetes treated with insulin had higher event rates, but there was no significant interaction of treatment and insulin requirement for the primary endpoint ($P_{interaction} = 0.40$), even after adjusting for SYNTAX score: the NNT with CABG vs. PCI to prevent one event was 12.7 for insulin-treated patients and 13.2 in those not requiring insulin.[279]

VACARDS (Veterans Affairs Coronary Artery Revascularization in Diabetes Study) compared CABG with PCI in patients with diabetes and extensive CAD in the USA.[154] Only 198 patients with diabetes were randomized due to early termination of the study. The combined risk of death or non-fatal MI was 18.4% for the CABG arm and 25.3% for the PCI arm (HR 0.89, 95% CI 0.47–1.71, $P < 0.05$).[154]

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In the CARDia (Coronary Artery Revascularization in Diabetes) trial, 510 patients with diabetes and multivessel or complex single-vessel CAD were randomly assigned to either CABG or PCI, with the use of either BMS or DES and routine use of abciximab.[156] There were no differences between CABG and PCI for the primary endpoint of 1 year composite of death, MI, or stroke, but the trial was underpowered to detect these differences. However, repeat revascularization was more likely to occur in patients treated with PCI (P <0.001).[156]

In the subset of 452 patients with diabetes and multivessel CAD who were enrolled in the SYNTAX trial, there were no differences in the composite safety endpoint of all-cause death, stroke, and MI at 5 year follow-up.[155] However, the need for repeat revascularization (HR 2.01, 95% CI 1.04–3.88, P <0.001) was significantly more frequent in patients with diabetes treated with PCI than in those who underwent CABG.[155,275] Patients with diabetes had a higher rate of repeat revascularization after PCI when compared with CABG in the low (≤22) (38.5 vs. 18.5%, respectively, P = 0.014) and intermediate (23 - 33) (27 vs. 13.4%, respectively, P = 0.049) SYNTAX score tertiles. Further analyses according to treatment with either oral hypoglycaemic agents or insulin showed that the MACCE rate was significantly greater after PCI in both the oral hypoglycaemic agent group (PCI 40.4 vs. CABG 26.4%, P = 0.022) and the insulin-dependent group (PCI 56.2 vs. CABG 32.6%, P = 0.002). A higher incidence of cardiac death was noted in the insulin-dependent patients treated with PCI (PCI 18.8 vs. CABG 7.1%, P = 0.023).

In the SYNTAX trial, diabetes was not an independent predictor of outcomes once the SYNTAX score was entered into the multivariable model.[127] Consequently, the SYNTAX 2 score does not include diabetes as one of the eight variables that impacts on the preferential selection of revascularization modality.[127] Conflicting data were seen in a patient-level pooled analysis of 6081 patients treated with stents (75% newer generation DES), stratified according to diabetes status and SYNTAX score.[157] After Cox regression adjustment, SYNTAX score and diabetes were both associated with MACE (P <0.001 and P = 0.0028, respectively). At 2 years, patients with diabetes had higher MACE (HR 1.25, 95% CI 1.03–1.53, P = 0.026) and TVR, and similar death and MI rates.[157]

In the BEST trial, patients with diabetes treated with PCI had a higher rate of the primary endpoint of death, MI, or TVR compared with CABG (EES: n=177; CABG: n=186) (19.2 vs. 9.1%, P = 0.007) (see section 5).[105]

9.2.2 Meta-analysis of coronary artery bypass grafting vs. percutaneous coronary intervention in patients with diabetes

A meta-analysis—restricted to four RCTs covering 3052 patients-compared PCI with the use of early-generation DES vs. CABG in patients with diabetes and multivessel CAD. It suggested a higher risk of death and MI with revascularization by early-generation DES (RR 1.51, 95% CI 1.09–2.10; P <0.01), but a lower risk of stroke (2.3 vs. 3.8%; RR 0.59, 95% CI 0.39– 0.90; P <0.01).[152] A sensitivity analysis revealed that this superiority of CABG over early-generation DES for the endpoint MACCE was most pronounced among patients with a high SYNTAX score. A network meta-analysis had suggested that the survival benefit of CABG over PCI in patients with diabetes might be lost when using EES,[151] though this was not confirmed in a subsequent meta-analysis that also included the direct comparison between EES and CABG in the subset of BEST.[153]

In a collaborative, individual patient data pooled analysis of 11 518 patients with multivessel or LM disease randomized to CABG or PCI with stents, all-cause death was significantly different after CABG (9.2%) and PCI (11.2%) (P = 0.0038), which was evident in patients with diabetes (10.7 vs. 15.7%, respectively; P = 0.0001) but not in patients without diabetes (8.4 vs. 8.7%, respectively; P = 0.81) ($P_{interaction}$ = 0.0077).[124] Similar results were found in the subgroup of 7040 patients with multivessel disease ($P_{interaction}$ = 0.0453), while the interaction with diabetes was not significant in the 4478 patients with LM disease ($P_{interaction}$ = 0.13).

A recent population-based analysis has confirmed the benefit of CABG compared with PCI in patients with diabetes when patients present with an ACS.[196] Consequently, overall current evidence continues to favour CABG as the revascularization modality of choice for patients with diabetes and multivessel disease. When patients present with a comorbidity that increases surgical risk, the choice of revascularization method is best decided by multidisciplinary individualized risk assessment.

9.3 Revascularization with the use of percutaneous coronary intervention

For the reasons discussed above, PCI in patients with diabetes is often more complex than PCI in the absence of diabetes. Nevertheless, irrespective of diabetic status, the same principles apply as discussed in section 16. Placement of a new-generation DES is the default strategy.

9.4 Antithrombotic pharmacotherapy

In the current context of the use of oral $P2Y_{12}$-inhibitors, there is no indication that antithrombotic pharmacotherapy should differ between diabetics and patients without diabetes who are undergoing revascularization. For detailed discussion refer to section 17.

9.5 Metformin

There is a theoretical risk of lactic acidosis and deteriorating renal function in patients treated with metformin who are exposed to iodinated contrast media.[280] Consequently, it is generally recommended that in elective cases, metformin should be withheld before angiography or PCI for 48 h, as the plasma half-life of metformin is 6.2 h,[280] and reintroduced 48 h later. However, clinical experience suggests that the actual risk of lactate acidosis is very small, and that checking renal function after angiography in patients on metformin and withholding the drug when renal function deteriorates appears to be an acceptable alternative.[280] In patients with renal failure, metformin should be stopped before the procedure. Accurate recognition of metformin-associated lactic acidosis based on arterial pH <7.35, blood lactate >5 mmol/L (45 mg/dL), and detectable plasma metformin concentration should prompt the initiation of haemodialysis.

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Recommendation for patients on metformin

Recommendation	Class[a]	Level[b]
It is recommended to check renal function if patients have taken metformin immediately before angiography and withhold metformin if renal function deteriorates.	I	C

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[a]Class of recommendation.
[b]Level of evidence.

9.6 Gaps in the evidence

Following successful revascularization, the rate of events during follow-up remains high in patients with diabetes, independent of the mode of revascularization. Future research should be focused on identifying new disease-modifying therapies to influence the progression of vascular disease in this high-risk cohort.

10 Revascularization in patients with chronic kidney disease

10.1 Evidence base for revascularization and recommendations

Myocardial revascularization in patients with chronic kidney disease (CKD), specifically National Kidney Foundation stage 3 or higher, is addressed by the 2014 ESC/EACTS Guidelines on myocardial revascularization. After reviewing the subsequent literature, the current Task Force has not found any evidence to support a major update. A recent *post hoc* analysis of the SYNTAX trial on patients with CKD confirms the principles for allocating patients to PCI or CABG,[281] as discussed in section 5 of this document.

10.2 Prevention of contrast-induced nephropathy

The risk of contrast-induced nephropathy (CIN) depends on patient-related factors, such as CKD, diabetes mellitus, congestive HF, haemodynamic instability, reduced plasma volume, female sex, advanced age, anaemia, and periprocedural bleeding, as well as on the type and volume of contrast administered.[282–288] When the ratio of total contrast volume (in mL) to glomerular filtration rate (in mL/min) exceeds 3.7, the risk of CIN increases significantly.[287,288]

Adequate hydration remains the mainstay of CIN prevention.[289–294] High-dose statins, as indicated for secondary prevention irrespective of the risk of CIN are also beneficial.[293] All other strategies for the prevention of CIN do not have sufficient evidence to justify a recommendation in favour or against.[293,294] For more detailed discussion refer to the Supplementary Data.

10.3 Gaps in the evidence

Thus far, patients with CKD have been excluded from randomized trials on myocardial revascularization, hence current data are based on observational studies only. A randomized trial on optimal long-term revascularization strategies in patients with moderate-to-severe stress-induced ischaemia and severe CKD is currently ongoing (ISCHEMIA-CKD, https://clinicaltrials.gov/ct2/show/NCT01985360). Moreover, additional randomized evidence on optimal strategies for CIN prevention is needed.

Recommendations for the prevention of contrast-induced nephropathy

Recommendations	Dose	Class[a]	Level[b]
Patients undergoing coronary angiography or MSCT			
It is recommended that all patients are assessed for the risk of contrast-induced nephropathy.		I	C
Adequate hydration is recommended.		I	C
Patients with moderate or severe CKD (National Kidney Foundation stages 3b and 4)			
Use of low-osmolar or iso-osmolar contrast media is recommended.[284–286]		I	A
It is recommended that the volume of contrast media be minimized.[287,288]	Total contrast volume/GFR <3.7.[c]	I	B
In statin-naïve patients, pre-treatment with high-dose statins should be considered.[293]	Rosuvastatin 40/20 mg or atorvastatin 80 mg.	IIa	A
Pre- and post-hydration with isotonic saline should be considered if the expected contrast volume is >100 mL.	1 mL/kg/h 12 h before and continued for 24 h after the procedure (0.5 mL/kg/h if LVEF ≤35% or NYHA >2).	IIa	C
As an alternative to the pre- and post- hydration regimen, tailored hydration regimens[d] may be considered.[295–297]		IIb	B

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Patients with severe CKD (National Kidney Foundation stage 4)			
Prophylactic haemofiltration 6 h before complex PCI may be considered.[298–300]	Fluid replacement rate 1000 mL/h without negative loss and saline hydration continued for 24 h after the procedure.	IIb	B
Haemodialysis is not recommended as a preventive measure.[300,301]		III	B

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CKD = chronic kidney disease; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; MSCT = multi-slice computed tomography; NYHA = New York Heart Association; PCI = percutaneous coronary angiography.
[a]Class of recommendation.
[b]Level of evidence.
[c]Example: 370 mL of contrast medium in a patient with a GFR of 100 mL/min will yield a ratio of 3.7.
[d]Options are: infusion of normal saline adjusted to central venous pressure[295] or furosemide with matched infusion of normal saline[296,297] (for details see the Supplementary Data).

11 Revascularization in patients requiring valve interventions

11.1 Primary indication for valve interventions

Myocardial revascularization in patients undergoing primary valve interventions, either by surgery or transcatheter routes, is addressed by the 2014 ESC/EACTS Guidelines on myocardial revascularization. After reviewing the subsequent literature, the current Task Force endorses the recommendations of the 2014 Guidelines and has not found any evidence to support a major update. These recommendations are included below for ease of reference. Of note, the available evidence on invasive functional assessment of CAD (with FFR or iwFR) in patients with severe aortic stenosis (AS) is limited to a few small-scale observational studies. These studies support the feasibility of FFR and iwFR in this setting.[302–304] Notwithstanding, the available evidence is insufficient to support the use of invasive functional assessment of coronary lesions in patients with AS, particularly in consideration of the altered haemodynamic condition related to the presence of AS. Therefore, the Task Force is in consensus that indications for myocardial revascularization based on angiographic assessment of CAD should be maintained, consistent with the 2014 ESC/EACTS Guidelines on myocardial revascularization and the 2017 ESC/EACTS Guidelines for the management of valvular heart disease.[305]

11.2 Primary indication for myocardial revascularization

11.2.1 Aortic valve disease

The recommendations for patients undergoing CABG for the clinically leading problem of CAD, who also have coexisting severe aortic stenosis or regurgitation, remain unchanged from those of the 2014 Guidelines and support replacement of the aortic valve.[305] However, in the current era of rapid developments in transcatheter valve implantation technologies, a decision regarding replacement of the aortic valve for moderate stenosis/regurgitation should be carefully considered on a case-by-case basis in discussion with the Heart Team. The patient's age, type of prosthesis, pathogenesis of aortic stenosis/regurgitation, aortic annular size, predicted size of implanted valve, transcatheter aortic valve implantation (TAVI) access routes, and technical feasibility of a TAVI procedure in the future in case of disease progression should all be taken into account.[306]

11.2.2 Mitral valve disease

Patients with concomitant severe primary mitral regurgitation (MR) should undergo mitral valve repair at the time of CABG in keeping with guidance for the surgical repair of primary MR.[305] There is also consensus based on expert opinion on the surgical repair of severe secondary MR at the time of CABG.[305,307] However, considerable controversy exists about the treatment of moderate secondary or ischaemic MR in patients undergoing CABG. Until the publication of 2 year outcomes of the CTSN (Cardiothoracic Surgical Trials Network) randomized trial on treatment of 'moderate' ischaemic MR, the literature in this field was limited to small single-centre randomized trials, observational studies, and case series, and failed to provide clear direction. The CTSN trial showed that addition of surgical mitral valve repair to CABG made no significant difference to survival, overall reduction of adverse events, or LV reverse remodelling at 2 years.[308,309] Increased length of intensive care and hospital stay and perioperative morbidity, including neurological complications and supraventricular arrhythmias, were reported in the CTSN and other randomized trials in this group of patients.[308–310] Because the CTSN trial used a very broad definition of moderate MR, including an effective regurgitant orifice area (EROA) $\leq$0.2 cm^2 plus additional criteria, no firm conclusions can be drawn concerning patients with an EROA >0.2 cm^2. Observational data suggest that in secondary MR, an EROA >0.2 cm^2 and regurgitant volume >30 mL indicates greater risk of cardiovascular events.[311,312] In the absence of dedicated trials in this setting, the decision to combine mitral valve surgery with CABG in patients with an EROA >0.2 cm^2 and regurgitant volume >30 mL needs to be made on a case-by-case basis by the Heart Team. For a more detailed discussion of this issue, please refer to the Supplementary Data.

11.3 Gaps in the evidence

In patients with concomitant valvular and coronary disease, the possibility of future transcatheter therapy for the aortic and mitral valves has made a significant impact on decision-making for patients with predominantly coronary disease with moderate valve lesions. However, there is currently little evidence on this topic. The need

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for and timing of PCI in patients undergoing TAVI is also an area with limited evidence. The long-term outcomes of patients with concomitant surgical repair of ischaemic MR are also awaited.

Recommendations for combined valvular and coronary interventions

Recommendations	Class[a]	Level[b]
Primary valve intervention and coronary revascularization		
CABG is recommended in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis >70%.	I	C
CABG should be considered in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis of 50–70%.	IIa	C
PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis >70% in proximal segments.	IIa	C
PCI should be considered in patients with a primary indication to undergo transcatheter mitral valve interventions and coronary artery diameter stenosis >70% in proximal segments.	IIa	C
Primary myocardial revascularization and valve intervention		
SAVR is indicated in patients with severe AS undergoing CABG, or surgery of the ascending aorta or another valve.	I	C
Mitral valve surgery is indicated in patients with severe[c] secondary MR undergoing CABG and LVEF >30%.	I	C
Mitral valve surgery should be considered in symptomatic patients with severe[c] secondary MR and LVEF <30%, but with evidence of myocardial viability and an option for surgical revascularization.	IIa	C

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AS = aortic stenosis; CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.
[a]Class of recommendation.
[b]Level of evidence.
[c]Severe secondary MR was defined as an effective regurgitant orifice area >0.40 cm^2.

12 Associated peripheral artery diseases

12.1 Prevention of stroke associated with carotid artery disease and myocardial revascularization

The early risk of stroke after myocardial revascularization is higher after CABG than after PCI.[313] After 30 days, stroke rates between revascularization techniques were similar in a recent individual patient data meta-analysis of 11 randomized trials.[313]

Ischaemic stroke after CABG is multifactorial: thrombo-embolism from the aorta, its branches, or the heart; atrial arrhythmias; inflammatory pro-thrombogenic milieu; lower levels of antiplatelet therapy perioperatively; and haemodynamic instability. However, the most consistent predictor of perioperative stroke is previous stroke or TIA. There is no strong evidence that carotid artery stenosis is a significant cause of perioperative stroke except for bilateral severe carotid bifurcation stenosis.[314] Therefore, indications for preoperative carotid bifurcation screening by duplex ultrasound are limited.[315] Also, there is no evidence that prophylactic revascularization of unilateral asymptomatic carotid stenoses in CABG candidates reduces the risk of perioperative stroke. It may be reasonable to restrict prophylactic carotid revascularization to patients at highest risk of postoperative stroke, i.e. patients with severe bilateral lesions or a history of prior stroke/TIA.[316] Hence, the indication for revascularization, and the choice between carotid endarterectomy or carotid artery stenting in these patients, should be made by a multidisciplinary team including a neurologist.

The 2017 Guidelines on the diagnosis and treatment of peripheral arterial diseases in collaboration with the European Society of Vascular Surgery cover the screening for and management of carotid artery disease in patients scheduled for CABG, including screening, indications, and the timing and type of carotid revascularization.[317] Its recommendations are reproduced here.

Particularly for patients at high risk for perioperative stroke after CABG, such as elderly patients or patients with previous TIA/stroke, specific preventive measures have been suggested. CT scan screening of the ascending aorta/arch atheroma has been proposed to better assess risk stratification and guide the surgical strategy in elderly patients.[318] It is recommended that acetylsalicylic acid is restarted 6 h, or at the latest 24 h, after surgery, and that clopidogrel or ticagrelor are added in patients with ACS. New-onset atrial fibrillation (AF) is associated with a risk of stroke that increased two-to-three times after CABG. Its management is discussed in section 14.

12.2 Associated coronary and peripheral artery diseases

Of all patients with CAD, 7–16% have lower extremity artery disease (LEAD), which is associated with a worse prognosis, even if it remains frequently asymptomatic, masked by cardiac symptoms. On the other hand, in patients with LEAD, CAD is present in up to 70% of patients.[317] The choice between CABG and PCI is controversial and, in the absence of solid data, it should follow a multidisciplinary

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approach.[127] In patients undergoing CABG, the saphenous vein should be preserved or harvested guided by the results of clinical examination including the ankle-brachial index. In addition, inter-arm blood pressure asymmetry should lead to the investigation of subclavian artery stenosis. Further details are provided in the 2017 peripheral arterial diseases Guidelines.[317]

Recommendations on the management of carotid stenosis in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients scheduled for CABG, it is recommended that the indication (and if so the method and timing) for carotid revascularization be individualized after discussion within a multidisciplinary team, including a neurologist.	I	C
In patients scheduled for CABG, with recent (<6 months) history of TIA/stroke:		
• Carotid revascularization should be considered in patients with 50 - 99% carotid stenosis.[319,320]	IIa	B
• Carotid revascularization with CEA should be considered as first choice in patients with 50 - 99% carotid stenosis.[319,320]	IIa	B
• Carotid revascularization is not recommended in patients with carotid stenosis <50%.	III	C
In neurologically asymptomatic patients scheduled for CABG:		
• Carotid revascularization may be considered in patients with bilateral 70 - 99% carotid stenosis or 70 - 99% carotid stenosis and contralateral occlusion.	IIb	C
• Carotid revascularization may be considered in patients with a 70 - 99% carotid stenosis, in the presence of one or more characteristics that may be associated with an increased risk of ipsilateral stroke,[c] in order to reduce stroke risk beyond the perioperative period.	IIb	C
• Routine prophylactic carotid revascularization in patients with a 70 - 99% carotid stenosis is not recommended.	III	C

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CABG = coronary artery bypass grafting; CEA = carotid endarterectomy; TIA = transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.
[c]Contralateral TIA/stroke, ipsilateral silent infarction on cerebral imaging, intraplaque haemorrhage or lipid-rich necrotic core on magnetic resonance angiography, or any of the following ultrasound imaging findings: stenosis progression (>20%), spontaneous embolization on transcranial Doppler, impaired cerebral vascular reserve, large plaques, echolucent plaques, or increased juxta-luminal hypoechogenic area.[317]

Preoperative strategies to reduce the incidence of stroke in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients undergoing CABG, carotid DUS is recommended in patients with recent (<6 months) history of stroke/TIA.[321,322]	I	B
In patients with no recent (<6 months) history of TIA/stroke, carotid DUS may be considered before CABG in the following cases: age ≥70 years, multivessel coronary artery disease, concomitant LEAD, or carotid bruit.[321,322]	IIb	B
Screening for carotid stenosis is not indicated in patients requiring urgent CABG with no recent stroke/TIA.	III	C

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CABG = coronary artery bypass grafting; DUS = duplex ultrasound; LEAD = lower extremity artery disease; TIA = transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.

13 Repeat revascularization

13.1 Early graft failure

Early graft failure after CABG is reported in up to 12% of grafts, as evaluated by intraoperative angiography.[323] However, only a minority (around 3%) are clinically apparent. Graft failure can be due to conduit defects, anastomotic technical errors, poor native vessel run-off, or competitive flow with the native vessel. When clinically relevant, acute graft failure may result in MI with consequently increased mortality and major cardiac events. The suspicion of early graft failure should arise in the presence of ECG signs of ischaemia, ventricular arrhythmias, biomarker changes, new wall motion abnormalities, or haemodynamic instability.[324,325] Owing to the low specificity of ECG changes and echocardiographic wall motion abnormalities during the post-operative course, and the delay in the appearance of biomarker changes, a careful assessment of all variables will influence decision-making for angiographic evaluation.

Perioperative angiography is recommended in cases of suspected severe myocardial ischaemia to detect its cause and aid decision-making on the most appropriate treatment.[323,325,326] In symptomatic patients, early post-operative graft failure can be identified as the cause of ischaemia in 40 - 80% of cases.[324,326–328] The optimal treatment strategy in patients with acute graft failure should be decided by *ad hoc* consultation between the cardiovascular surgeon and the interventional cardiologist, on the basis of the patient's clinical condition and the extent of myocardium at risk. In the case of early post-operative graft failure, emergency *ad hoc* PCI may limit the extent of infarction, if technically feasible. The target for PCI is the native vessel or the internal mammary artery (IMA) graft, while the acutely

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occluded saphenous vein graft (SVG) and any anastomotic site should be avoided, if possible, due to concerns regarding embolization or perforation. Redo surgery should be favoured if the anatomy is unsuitable for PCI, if several important grafts are occluded, or in the case of clear anastomotic errors. In asymptomatic patients, repeat revascularization should be considered if the artery is of an appropriate size and supplies a large territory of myocardium.

Further details on the diagnosis and management of perioperative MI are provided in a recent ESC position paper.[329]

13.2 Acute percutaneous coronary intervention failure

The need for urgent surgery to manage PCI-related complications is uncommon (<1%) and only required in patients with major complications that cannot be adequately resolved by percutaneous techniques.[330,331] The need for emergency CABG is mainly confined to patients with a large, evolving MI due to iatrogenic vessel occlusion that cannot be salvaged percutaneously, or in patients with recurrent cardiac tamponade after pericardiocentesis following PCI-related vessel rupture.[330,332,333]

13.3 Disease progression and late graft failure

Ischaemia after CABG may be due to the progression of disease in native vessels or *de novo* disease of bypass grafts.[334] Repeat revascularization in these patients is indicated in the presence of significant symptoms despite medical treatment, and in asymptomatic patients with objective evidence of large myocardial ischaemia (>10% of the LV).[32,87]

13.3.1 Redo coronary artery bypass grafting or percutaneous coronary intervention

PCI in patients with prior CABG has worse acute and long-term outcomes than in patients without prior CABG.[335,336] Likewise, redo CABG has a two- to four-fold increased mortality compared with first-time CABG, and repeat CABG is generally performed infrequently.[334,337–339] There are limited data comparing the efficacy of PCI vs. redo CABG in patients with previous CABG. The proportion of patients undergoing PCI, redo CABG, or conservative treatment differs significantly between studies; in one study, PCI was favoured in ~50% of patients with only 22% undergoing redo CABG, while another study favoured CABG in 67% of patients.[340,341] In the AWESOME (Angina With Extremely Serious Operative Mortality Evaluation) RCT and registry, overall 3 year mortality was comparable between redo CABG and PCI.[341,342] A more recent study also found comparable rates of death and MI between redo CABG and PCI, although there were significantly more repeat revascularizations with PCI.[341,343]

In view of the higher risk of procedural mortality with redo CABG and the similar long-term outcome, PCI is the preferred revascularization strategy in patients with amenable anatomy.[340] PCI via the bypassed native artery should be the preferred approach. If PCI in the native vessel fails or is not an option, PCI in the diseased SVG should be considered. CABG should be considered for patients with extensively diseased or occluded bypass grafts and diffuse native vessel disease, especially in the absence of patent arterial grafts.[340] The IMA is the conduit of choice for revascularization during redo CABG if not previously used, or can be salvaged and reused in specific cases.[344,345]

13.3.2 Percutaneous coronary intervention for saphenous vein graft lesions

PCI in SVGs is associated with an increased risk of distal coronary embolization, frequently resulting in periprocedural MI.[346] PCI of *de novo* SVG stenosis is considered a high-risk intervention because SVG atheroma is friable and more prone to distal embolization. Several different approaches have been evaluated to prevent the distal embolization of particulate debris, including distal occlusion/aspiration, proximal occlusion, suction, filter devices, or covered stents. Distal protection devices using filters have shown the most encouraging results. However, although a single randomized trial supports the use of distal embolic protection during SVG PCI, observational studies including data from large-scale registries are conflicting.[347–349] Outcomes from studies with other devices used for SVG PCI are not sufficient to recommend its use.[350–353]

Based on data from a small number of randomized trials, implantation of DES in SVG lesions is associated with a lower risk of repeat revascularization than with BMS at 1 year follow-up.[354–356] In the only trial powered for a clinical endpoint—the ISAR-CABG (Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts) trial[354]—the primary endpoint of death, MI, and target lesion revascularization was significantly reduced with DES vs. BMS. However, at 5 year follow-up, the advantage of DES over BMS was lost due to a higher incidence of target lesion revascularization between years 1 and 5 in patients treated with DES.[357] Longer-term follow-up of the two smaller trials is available; one suggested sustained superiority of DES over BMS, while the other suggested loss of the efficacy advantage of the DES.[358,359]

13.4 Repeat percutaneous coronary intervention

Recurrence of symptoms or ischaemia after PCI is the result of restenosis, incomplete initial revascularization, or disease progression.[334] Patients may require repeat PCI due to late and very late stent thrombosis.

13.4.1 Restenosis

Restenosis associated with angina or ischaemia should be treated by repeat revascularization, and repeat PCI remains the strategy of choice for most of these patients. In this setting, the results from DES are superior to those obtained with balloon angioplasty, BMS implantation, or brachytherapy.[360–364]

For restenosis within BMS, drug-coated balloon (DCB) proved superior to plain balloon angioplasty[365–367] and comparable to first-generation DES.[365,366,368–372] One trial showed inferior angiographic outcomes in comparison to new-generation DES,[373] while a second trial showed comparable outcomes.[374] For restenosis within DES, DCBs also proved superior to plain balloon angioplasty[367,369,371] and comparable to first-generation DES.[371] In one study, DCBs were inferior to new-generation DES in terms of the primary angiographic outcome measure.[375] In a more recent study, including patients with any type of in-stent restenosis, outcomes between DCB and repeat

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stenting with new-generation DES were comparable.[376] A single randomized trial of patients undergoing DCB for restenosis within DES showed superior angiographic outcomes in patients who underwent lesion preparation with scoring balloons vs. standard angioplasty balloons.[377]

Network meta-analysis suggests that repeat stenting with new-generation DES (with EES) and DCB are ranked first and second as the highest efficacy treatments.[378,379] The superior angiographic antirestenotic efficacy of new-generation DES should be weighed against a possible excess of long-term adverse events with repeat stenting during longer-term follow-up of these trials.[380,381] However, observations in relation to clinical events must be interpreted with caution, as none of the trials was powered for clinical endpoints and the comparator stent in studies with long-term follow-up was an early-generation DES.

The use of intracoronary imaging provides unique insights into the underlying mechanisms of in-stent restenosis (see section 16.2). OCT is able to detect the presence of neoatherosclerosis in a significant number of these patients. Underexpanded stents should be aggressively tackled with high-pressure dilatations using non-compliant balloons. The optimization of the final results remains crucial during reinterventions for in-stent restenosis and, in this regard, the use of intracoronary imaging may be particularly helpful. Outcomes of patients with in-stent restenosis after DES are poorer than those in patients with BMS in-stent restenosis, independently of the therapeutic modality.[382] In patients with recurrent episodes of diffuse in-stent restenosis in large vessels—and in those with associated multivessel disease, especially in the presence of other complex lesions such as chronic total occlusions—CABG should be considered before a new PCI attempt.

13.4.2 Disease progression

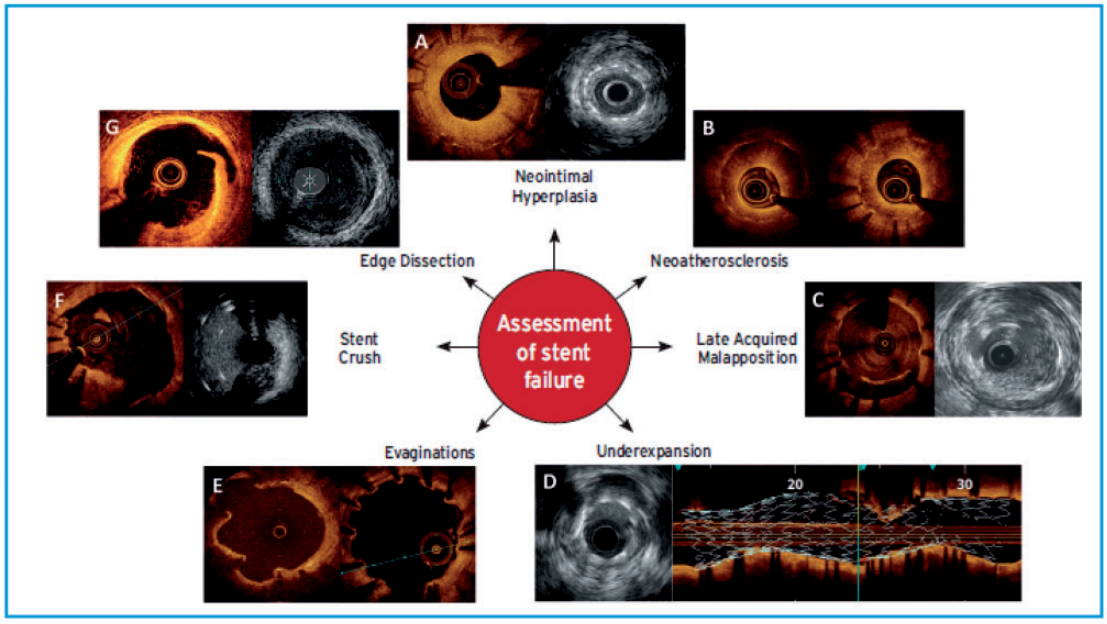
Patients with symptomatic disease progression after PCI account for up to 50% of reinterventions.[383,384] They should be managed using criteria similar to those applied to patients without previous revascularization.

13.4.3 Stent thrombosis

Although stent thrombosis is very rare, particularly since the advent of new-generation DES, it may have devastating clinical consequences. Stent thrombosis usually presents as a large MI and patients should be treated according to the principles outlined in section 8.[385] Aggressive, high-pressure balloon dilation should be used to correct underlying, stent-related, predisposing mechanical problems.[386,387] Liberal use of intracoronary imaging in order to detect and modify underlying mechanical factors is recommended (*Figure 7*) (see section 16.2).

Although repeat stenting in patients with stent thrombosis may be avoided when satisfactory results are obtained with balloon dilation, a new stent may be required to overcome edge-related dissections and adjacent lesions, or to optimize final results.[388]

There is no evidence that the post-interventional management of patients with stent thrombosis should differ from that of patients with thrombosis of a *de novo* lesion resulting in STEMI.



Examples of intravascular imaging findings (IVUS or OCT) in patients with stent failure. **Panel A** displays OCT (left) and IVUS (right) examples of in-stent restenosis due to excessive neointimal hyperplasia. **Panel B** displays two OCT examples of in-stent restenosis due to neoatherosclerosis. **Panel C** displays OCT (left) and IVUS (right) examples of late acquired malapposition. **Panel D** displays IVUS (left) and longitudinal OCT reconstruction (right) images of stent underexpansion. **Panel E** displays two OCT examples of in-stent evaginations, a typical finding of delayed arterial healing. **Panel F** displays OCT (left) and IVUS (right) examples of stent crush. **Panel G** displays an OCT (left) and IVUS (right) case of coronary dissection at the stent edge.
IVUS = intravascular ultrasound; OCT = optical coherence tomography.
Intracoronary images for this figure were kindly provided by Drs Nicolas Amabile, Fernando Alfonso, and Gennaro Sardella.

Figure 7 Intracoronary imaging for the assessment of stent failure.

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Recommendations on repeat revascularization

Recommendations	Class[a]	Level[b]
Early post-operative ischaemia and graft failure		
Coronary angiography post-CABG is recommended for patients with: • symptoms of ischaemia and/or abnormal biomarkers suggestive of perioperative MI • ischaemic ECG changes indicating large area of risk • new significant wall motion abnormalities • haemodynamic instability.	I	C
It is recommended that either emergency reoperation or PCI is decided upon by *ad hoc* consultation in the Heart Team, based on the feasibility of revascularization, area at risk, comorbidities, and clinical status.	I	C
Disease progression and late graft failure		
Repeat revascularization is indicated in patients with a large area of ischaemia or severe symptoms despite medical therapy.[84,334]	I	B
If considered safe, PCI should be considered as first choice over CABG.	IIa	C
Procedural aspects of the revascularization modalities		
CABG		
IMA is the conduit of choice for redo CABG in patients in whom the IMA was not used previously.[344]	I	B
Redo CABG should be considered for patients without a patent IMA graft to the LAD.[340,341,344]	IIa	B
PCI		
Distal protection devices should be considered for PCI of SVG lesions.[348,350,351]	IIa	B
PCI of the bypassed native artery should be considered over PCI of the bypass graft.	IIa	C
Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES.[373,375,378,379]	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

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BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; ECG = electrocardiogram; IMA = internal mammary artery; IVUS = intravascular ultrasound; LAD = left anterior descending artery; MI = myocardial infarction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; SVG = saphenous vein graft.
[a]Class of recommendation.
[b]Level of evidence.

14 Arrhythmias

14.1 Ventricular arrhythmias

14.1.1 Revascularization for the prevention of sudden cardiac death in patients with stable coronary artery disease and reduced left ventricular function

Revascularization plays an important role in reducing the frequency of ventricular arrhythmias in patients with normal or mildly reduced LV function,[389,390] as well as the risk of sudden cardiac death in patients with CAD and LVEF ≤35%.[391] Indirect evidence for a protective effect of revascularization was demonstrated in the MADIT II (Multicenter Automatic Defibrillator Implantation Trial II) and SCD-HEFT studies (Sudden Cardiac Death in Heart Failure Trial), where the efficacy of implantation cardioverter defibrillators (ICDs) was reduced if revascularization was performed prior to implantation.[392,393] CABG in patients with reduced EF reduces cardiac and overall mortality for a follow-up of 10 years.[78,81] In view of the protective effect of revascularization on ventricular arrhythmias, patients

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with ischaemic LV dysfunction (LVEF ≤35%) who are considered for primary preventive ICD implantation should be evaluated for ischaemia and/or for potential revascularization targets.

14.1.2 Revascularization for the treatment of electrical storm

Electrical storm is a life-threatening syndrome related to incessant ventricular arrhythmias, which is most frequently observed in patients with ischaemic heart disease, advanced systolic HF, valve disease, corrected congenital heart disease, and genetic disorders such as Brugada syndrome, early repolarization, and long QT syndrome.[394] Urgent coronary angiography and revascularization should be part of the management of patients with electrical storm, as well as antiarrhythmic drug therapy and/or ablation of ventricular tachycardia.

14.1.3 Revascularization after out-of-hospital cardiac arrest

Approximately 70% of survivors of out-of-hospital cardiac arrest have CAD, with acute vessel occlusion observed in 50%.[395] Multiple non-randomized studies suggest that emergency coronary angiography and, if appropriate, PCI after out-of-hospital cardiac arrest yield a favourable survival rate of ≤60% at 1 year, which is considerably higher than the 25% overall survival rate in patients with aborted cardiac arrest.[396,397] More recent data suggest that almost one-quarter of patients, resuscitated from cardiac arrest but without ST-segment elevation, show a culprit lesion (either vessel occlusion or irregular lesion).[398–401] Recent large-scale observational studies have shown an impact on mortality of early angiography after out-of-hospital cardiac arrest.[402,403] Thus, in survivors of out-of-hospital cardiac arrest, early coronary angiography and PCI, if appropriate, should be performed irrespective of the ECG pattern if no obvious non-cardiac cause of the arrhythmia is present.[404]

14.2 Atrial arrhythmias

The management of AF in patients with ischaemic heart disease is addressed by the 2016 ESC Guidelines for the management of AF developed in collaboration with EACTS.[405] After reviewing the subsequent literature, the current Task Force endorses the recommendations of the 2016 Guidelines and has not identified a need for any major update. Accordingly, the recommendation tables are taken from the 2016 Guidelines. For a detailed discussion, we refer to the previous Guidelines.[405]

14.2.1 Atrial fibrillation complicating percutaneous coronary intervention

New-onset AF in patients undergoing PCI occurs in 2–6% of procedures and increases with age, pre-existing HF, AMI, and arterial hypertension.[406–409] Notably, new-onset AF [defined as change from sinus rhythm (SR) at admission to AF during/after PCI] typically occurs during the first 4 days after AMI, and is associated with impaired prognosis and a more than doubling of the risk of death, congestive HF, and stroke.[403]

The use of oral anticoagulation (OAC) for stroke prevention in patients with AF occurring during or after PCI should follow the ESC Guidelines on Atrial Fibrillation for antithrombotic treatment of AF that occurs outside the setting of PCI,[405] although prospective studies are scarce. The combination and duration of anticoagulation and antiplatelet therapy should be assessed according to the clinical situation, as outlined in section 17 as well as in the ESC Guidelines on Atrial Fibrillation[405] and the ESC Focused Update on Dual Antiplatelet Therapy.[410]

14.2.2 Atrial fibrillation complicating coronary artery bypass grafting

Post-operative AF affects one-third of patients undergoing cardiac surgery.[411–414] The main risk factor for post-operative AF is age, and it is associated with an increased immediate risk of stroke, increased morbidity, and 30 day mortality.[415–417] In the long-term, patients with an episode of post-operative AF have a two-fold increase in cardiovascular mortality, and a substantially increased risk of future AF and ischaemic stroke compared with patients who remain in SR after surgery.[416,418–422]

Post-operative AF is a common complication, in which prophylactic treatment has a moderate effect. Pre-operative anti-arrhythmic drug treatment may be initiated but will have to be weighed against side effects. Beta-blockers decrease the incidence of post-operative AF after CABG.[412,423–429]

14.2.3 Post-operative atrial fibrillation and stroke risk

Patients with post-operative AF have an increased stroke risk post-operatively as well as during follow-up,[419,430] and warfarin medication at discharge has been associated with a reduced long-term mortality.[431] To date, there are no studies indicating that post-operative AF is less harmful than any other form of AF, and good quality data are needed. Anticoagulation treatment with warfarin or non-vitamin K antagonist oral anticoagulants (NOACs) for stroke prevention in patients with post-operative AF should therefore follow the guidelines for the antithrombotic treatment of AF occurring outside the setting of CABG using the CHA_2DS_2-VASc [Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled) – Vascular disease, Age 65–74 and Sex category (Female)] score. The duration and timing of OAC in post-operative AF patients should be assessed individually.

Whether or not surgical left atrial appendage (LAA) obliteration reduces stroke risk has been studied in smaller trials and registry studies with conflicting results,[432–434] and is currently under investigation in a large randomized trial.[435] Removal or closure of the LAA should be considered as an adjunct to anticoagulation and not as an alternative until more data are available.

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Recommendations for the prevention of ventricular arrhythmias by revascularization

Recommendations	Class[a]	Level[b]
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG consistent with STEMI.[395,397,436,437]	I	B
Urgent angiography (and PCI if indicated) should be considered in patients with resuscitated cardiac arrest without diagnostic ST-segment elevation but with a high suspicion of ongoing myocardial ischaemia.	IIa	C
In patients with electrical storm, urgent coronary angiography and revascularization (as required) should be considered.	IIa	C

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ECG = electrocardiogram; STEMI = ST-elevation myocardial infarction; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations for the prevention and treatment of atrial fibrillation in the setting of myocardial revascularization

Recommendations	Class[a]	Level[b]
Perioperative oral beta-blocker therapy is recommended for the prevention of post-operative AF after CABG surgery.[412,438]	I	B
Restoration of sinus rhythm by electrical cardioversion or antiarrhythmic drugs is recommended in post-operative AF with haemodynamic instability.	I	C
Perioperative amiodarone should be considered as prophylactic therapy to prevent AF after CABG surgery.[412,439]	IIa	A
Long-term anticoagulation should be considered in patients with AF after CABG or PCI who are at risk of stroke, considering the individual stroke and bleeding risk.[440,441]	IIa	B
Rate control and anticoagulation should be considered as the initial management of asymptomatic post-operative AF.[442]	IIa	B
Antiarrhythmic drugs should be considered for symptomatic post-operative AF after CABG or PCI in an attempt to restore sinus rhythm.	IIa	C
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing CABG surgery.[432–434]	IIb	B

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AF = atrial fibrillation; CABG = coronary artery bypass grafting; LAA = left atrial appendage; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

14.3 Gaps in the evidence

The duration of anticoagulation and their combination with antiplatelet therapy in patients with new-onset AF after PCI or CABG has not been studied sufficiently. Likewise, the role of routine left atrial exclusion at surgery for the prevention of stroke is currently unclear.

15 Procedural aspects of coronary artery bypass grafting

CABG remains the most common cardiac surgical procedure, and the techniques have been refined during 50 years of evolution.[443] Perioperative medication and blood management are covered in separate Guidelines.[410,444]

15.1 Surgical techniques

15.1.1 Completeness of revascularization

Current surgical practice is largely based on an anatomical definition of complete revascularization, and aims to bypass all epicardial vessels with a diameter exceeding ≥1.5 mm and a luminal reduction of ≥50% in at least one angiographic view.[131] Depending on the definition of completeness of revascularization, the outcome after CABG in patients with incomplete revascularization was either similar[445–449] or inferior[131,132,449–451] to that of patients with complete

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revascularization. Certainly, in some patients with a stenosis in small vessels with little myocardium at risk, complete revascularization may not be necessary.

FFR-guided surgical revascularization has been associated with improved graft patency, but more studies are needed to investigate whether it improves clinical outcomes.[28,452] Further discussion of FFR-guided revascularization is provided in sections 3.2.1.1 and 5.3.1.3.

15.1.2 Conduit selection

In addition to patient-related factors, the outcome following CABG is related to the long-term patency of grafts and therefore is maximized with the use of arterial grafts, specifically the IMA.[453,454] Except in rare circumstances, all patients should receive at least one arterial graft—the left IMA (LIMA)— preferentially to the LAD.[453,455] SVG patency rates for non-LAD targets have been reported to be suboptimal.[456] Bilateral IMA (BIMA) and radial artery for non-LAD targets have been shown to provide better patency rates than SVG, particularly for the left coronary artery system.[457] Therefore, a second arterial graft should be considered depending on the patient's life expectancy, risk factors for sternal wound complications, coronary anatomy, degree of target vessel stenosis, graft quality, and surgical expertise.

Whether or not the use of additional arterial grafts can translate into prolonged survival remains debatable. Data from non-randomized studies suggest that the use of BIMA over single IMA (SIMA) use is associated with improved long-term survival, as well as fewer non-fatal events such as MI, recurrent angina, and the need for re-operation.[458–465] However, observational studies are subject to selection bias, despite propensity matching, and the effect of prolonged survival with additional arterial grafts has not been confirmed in randomized trials.[466]

The ART trial (Arterial Revascularization Trial) has been designed to answer the question of whether BIMA can improve 10 year survival when compared with SIMA. Interim analysis showed no difference at 5 years in the rate of death or the composite of death, MI, or stroke, and 10 year results are warranted to draw final conclusions.[467] Limitations of the ART trial include a high crossover rate from the BIMA arm to the SIMA arm and a high rate of radial artery use in the SIMA arm that may have diluted the benefit of BIMA.[468–470] The use of BIMA grafting is associated with an increase in sternal dehiscence, and an increased rate of mediastinitis in obese patients and patients with diabetes.[458,464,471–475] In the ART trial, the use of BIMA was associated with a 1.0 - 1.5% absolute risk increase in the need for sternal would reconstruction, and a subsequent subanalysis has found that this risk is minimized with skeletonized harvesting.[476] While we await the 10 year data of the ART trial, BIMA grafting should be considered in patients with a reasonable life expectancy and a low risk of sternal wound complications.

The radial artery constitutes an alternative as the second arterial graft in patients in whom BIMA grafting is not feasible, patients with a high risk of sternal wound complications, or as a third arterial graft. There is a strong, adverse influence on radial artery patency when the native coronary artery stenosis is <70%, and therefore its use should be limited to coronary artery stenosis >70% and ideally >90%.[477] Use of the radial artery as the second conduit of choice has been linked to improved survival in registry studies.[478–480] Available RCTs testing the radial artery vs. saphenous vein graft used angiographic patency as the primary endpoint, and none was powered to detect differences in clinical outcomes.[481] A recently published patient-level meta-analysis pooling six RCTs comparing radial artery vs. saphenous vein graft showed that the use of the radial artery was associated with a lower rate of the primary endpoint (composite of death, myocardial infarction, and repeat revascularization) at mean follow-up of 50 months, mainly driven by a significantly strong reduction of need for reintervention and a more modest reduction in subsequent MI.[482] Despite a significantly lower risk of occlusion at follow-up angiography, no difference in all-cause mortality was found.

15.1.3 Mammary artery harvesting

While the skeletonized technique of harvesting the IMA has a higher theoretical potential for injury, the potential benefits include a longer conduit, more versatility (sequential anastomosis), higher blood flow, and fewer wound-healing problems.[471,483–488] Therefore, in patients at higher risk of sternal wound complications, skeletonization is recommended.

15.1.4 Radial artery harvesting

Radial artery harvesting is associated with negligible morbidity if preceded by assessment of the hand's collateral circulation. Endoscopic radial harvesting is possible, but robust evidence concerning its safety and efficacy is scarce.[489,490] Use of the radial artery after recent coronary angiography with radial access should be discouraged due to potential endothelial damage.[491] Harvesting of the whole radial artery pedicle, together with the intraluminal and subadventitial injection of vasodilators, are useful steps to prevent spasm.

15.1.5 Saphenous vein harvesting

Saphenous vein harvesting can be accomplished using open and minimally invasive techniques, which include interrupted incisions and partial or full endoscopic procedures. Endoscopic vein graft harvesting leads to a reduced rate of leg wound complications,[492–495] but the short- and long-term patency of endoscopically harvested vein grafts, compared with openly harvested grafts, has been challenged.[456,496–498] Although there is no unequivocal evidence

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concerning patency rates, most data from meta-analyses and randomized and non-randomized trials do not demonstrate inferior clinical outcomes with endoscopic vein harvest.[492,493,499,500] If an endoscopic vein graft harvest is performed, it should be undertaken by experienced surgeons or physician assistants with appropriate training and reasonable caseloads.[501–503] If an open technique is used, the 'no-touch' technique has shown superior patency rates in multiple randomized trials,[504–507] with a patency rate >80% after 16 years.[507]

15.1.6 Cross-Clamping

A single cross-clamp technique may be preferred to multiple manipulations of the aorta, with the aim of reducing atheroembolic events, but a strict no-touch technique most effectively reduces embolization of atherosclerotic material.[508–510] In cases of off-pump surgery, devices that allow a clampless procedure may help reduce the incidence of cerebral vascular complications.[511,512]

15.1.7 Intraoperative quality control

Besides continuous ECG monitoring and transoesophageal echocardiography immediately after revascularization, intraoperative quality control may also include graft flow measurement to confirm or exclude a technical graft problem.[513] Transit-time flow measurement is the most frequently used technique for graft assessment and has been able to detect 2 - 4% of grafts that require revision.[513,514] In observational studies, the use of intraoperative graft assessment has been shown to reduce the rate of adverse events and graft failure, although interpretation can be challenging in sequential and T-graft configurations.[513,515–517]

15.1.8 On-pump and off-pump procedures

Two large, international randomized trials have shown no difference in 30 day or 1 year clinical outcomes between on- and off-pump surgery when performed by experienced surgeons.[518–520] There is also evidence to conclude that, for most patients and surgeons, on-pump surgery provides excellent short- and long-term outcomes.[518,520–523] For some surgeons, off-pump surgery is associated with inferior early and late graft patency rates, and possibly compromised long-term survival; however, aortic no-touch/clampless off-pump procedures in the hands of highly trained teams appear to be associated with a reduced risk of early morbidity, such as stroke, and fewer transfusions.[508–510,524–528] In the subgroup of patients with end-stage CKD, there is some evidence that off-pump surgery is associated with lower in-hospital mortality and less need for new renal replacement therapy.[529]

A summary of these technical aspects can be found in *Figure 8*.

15.1.9 Minimally invasive and hybrid procedures

Minimally invasive coronary surgery with LIMA, harvested either directly or under video-assisted vision, may represent an attractive alternative to a sternotomy.[530] It has a similar safety and efficacy profile to conventional on-pump and off-pump procedures, with a markedly reduced post-operative length of stay and an early quality of life benefit, although spreading of the ribs is associated with increased post-operative pain.[531–533] It has been shown to be safe and effective in the treatment of proximal LAD stenosis or chronically occluded LAD arteries.[144] Moreover, when compared with PCI in a setting of single-vessel proximal LAD disease, minimally invasive coronary surgery was associated with less need for coronary reintervention.[143,534,535] When combined with PCI to non-LAD vessels, it provides the opportunity for hybrid coronary revascularization to be performed in selected patients with multivessel disease.[536]

Hybrid revascularization can be performed consecutively in a hybrid operating room, or sequentially on separate occasions in the conventional surgical and PCI environments.[537–540] In a small randomized trial of 200 patients, 1 year and 5 year rates of death, MI, stroke, and major bleeding or repeat revascularization were not significantly different between hybrid revascularization and CABG.[536,541] Heart Team discussion and the prospective planning of a joint strategy are critical for the success of a hybrid revascularization strategy.[542]

15.2 Reporting perioperative outcomes

Perioperative reporting of outcomes after CABG procedures should be done on a risk-adjusted basis. The early risk period after CABG extends up to 3 months, is multifactorial, and depends on the interface between technical variability and patient comorbidity.[543]

15.3 Gaps in the evidence

The role of FFR and iwFR in guiding surgical revascularization needs further investigation into whether it improves clinical outcomes. Likewise, there are insufficient data on the impact of intraoperative assessment of graft flow on outcomes.

In view of the limitations of observational studies comparing BIMA with SIMA and the limitations of the ART trial, the ROMA (Randomization of Single vs. Multiple Arterial Grafts) trial is recruiting to answer the question of whether the use of additional arterial conduits (either BIMA or radial artery) translates into superior clinical outcomes when compared with SIMA supplemented by SVG only.

Hybrid procedures, which combine minimally invasive arterial grafting with PCI, proved feasible and safe. However, multicentre studies are required to prove the efficacy and superiority of this approach in stable, multivessel coronary disease.

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Recommendations on procedural aspects of coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
General considerations		
Complete myocardial revascularization is recommended.[c] [131,132]	I	B
Minimization of aortic manipulation is recommended.[508,509,544,545]	I	B
Routine intraoperative graft flow measurement should be considered.[516,517]	IIa	B
CT scans of the ascending aorta should be considered in patients over 70 years of age and/or with signs of extensive generalized atherosclerosis.	IIa	C
Prior to aortic manipulation, epiaortic ultrasound should be considered to identify atheromatous plaques and select the optimal surgical strategy.	IIa	C
Conduit selection		
Arterial grafting with IMA to the LAD system is recommended.[453,454,546]	I	B
An additional arterial graft should be considered in appropriate patients.[467,482,547–551]	IIa	B
The use of the radial artery is recommended over the saphenous vein in patients with high-grade coronary artery stenosis.[d] [482,549,550,552,553]	I	B
BIMA grafting should be considered in patients who do not have a high risk of sternal wound infection.[e] [467,547,548,551]	IIa	B
Vessel harvesting		
Skeletonized IMA dissection is recommended in patients with a high risk of sternal wound infection.[471,484,485]	I	B
Endoscopic vein harvesting, if performed by experienced surgeons, should be considered to reduce the incidence of wound complications.[490,493,494,500,554]	IIa	A
No-touch vein harvesting should be considered when an open technique is used.[506,507,555,556]	IIa	B
Minimally invasive techniques		
Off-pump CABG and preferably no-touch techniques on the ascending aorta, by experienced operators, are recommended in patients with significant atherosclerotic aortic disease.[508,509,544,557–559]	I	B
Off-pump CABG should be considered for subgroups of high-risk patients by experienced off-pump teams.[525,557–560]	IIa	B
Where expertise exists, minimally invasive CABG through limited thoracic access should be considered in patients with isolated LAD lesions or in the context of hybrid revascularization.[143,534,535,561]	IIa	B
Hybrid procedures, defined as consecutive or combined surgical and percutaneous revascularization, may be considered in specific patient subsets at experienced centres.[536,561–563]	IIb	B

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BIMA = bilateral internal mammary artery; CABG = coronary artery bypass grafting; CT = computed tomography; IMA = internal mammary artery; LAD = left anterior descending coronary artery.
[a]Class of recommendation.
[b]Level of evidence.
[c]Definitions of complete revascularization are provided in section 5.3.1.3.
[d]Particularly in patients with poor vein grafts. The radial artery should not be used if previously catheterized, if the Allen test is positive or if calcific degeneration is present.
[e]Patients with diabetes mellitus, chronic pulmonary obstructive disease, previous mediastinal radiation, and obesity, particularly when multiples of these are present.

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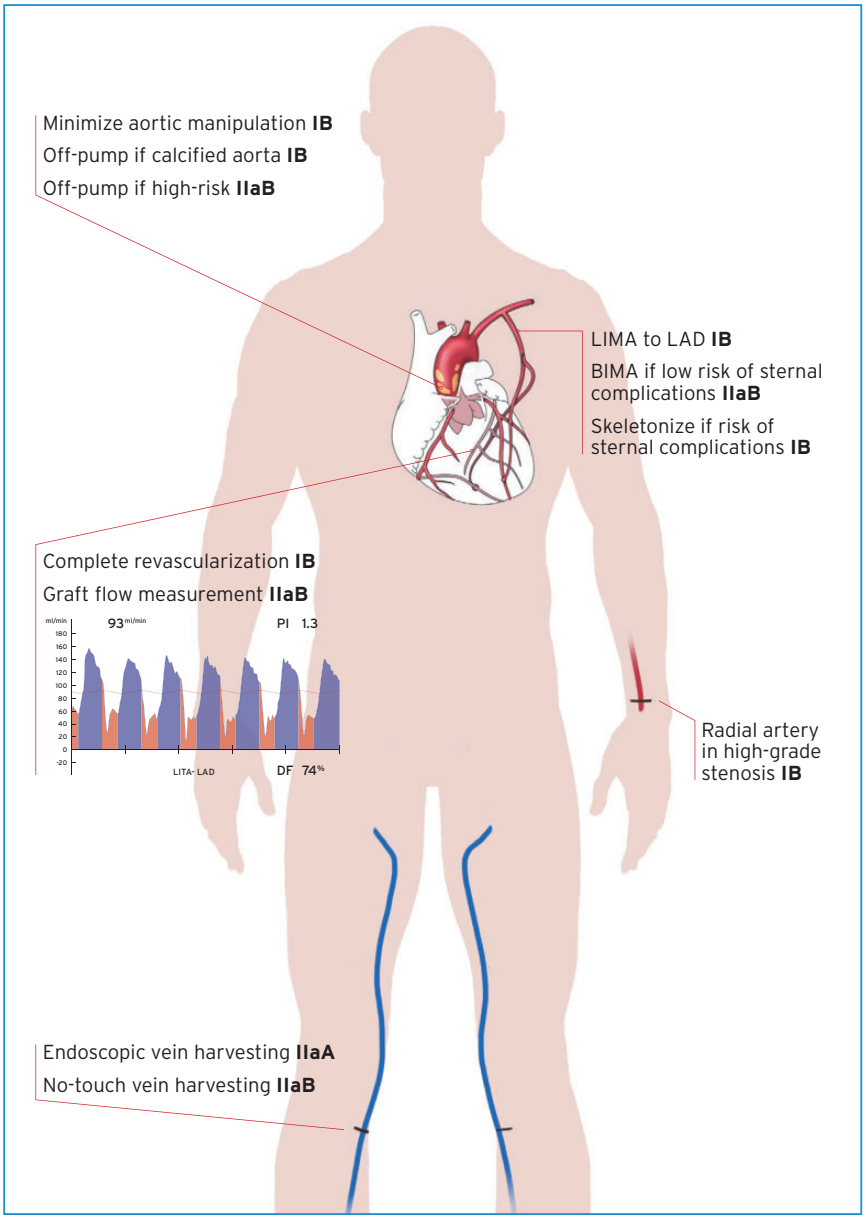

Figure 8 Technical aspects of CABG. BIMA = bilateral internal mammary artery; CABG = coronary artery bypass grafting; IMA = internal mammary artery; LAD = left anterior descending coronary artery.

16 Procedural aspects of percutaneous coronary intervention

16.1 Percutaneous coronary intervention devices

16.1.1 Balloon angioplasty

Plain balloon angioplasty has been superseded in the treatment of *de novo* coronary lesions after demonstration of the superiority of stenting in terms of the requirement for repeat revascularization.[564] Balloon angioplasty might be considered for the treatment of selected patients in whom implantation of stents is not technically feasible, or in a vessel that is considered to be too small to be stented. Balloon angioplasty is no longer preferred to stenting with DES for patients who require urgent non-cardiac surgery as short-duration DAPT may be reasonable with both strategies.[565,566]

16.1.2 Choice of coronary stents

Stenting with BMS results in an approximately 30% lower rate of restenosis in comparison with plain balloon angioplasty.[564] Although many efforts have been made to further reduce restenosis by the modification of stent designs and materials, reducing the thickness of stent struts has been the only proven modification capable of reducing restenosis of BMS.[567,568]

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A major reduction in the risk of restenosis has been achieved with DES technology. Early-generation DES released sirolimus[569] or paclitaxel[570] from a permanent polymer matrix coating on a relatively thick-strut (120–140 μm) stainless steel backbone. These devices reduced angiographic and clinical restenosis by approximately 50–70%, but increased the risk of very late stent thrombosis compared with BMS.[336,571]

Early-generation DES have now been supplanted by new-generation DES. These stents represented an iterative development of early generation technology, including polymers with enhanced biocompatibility (permanent or biodegradable), exclusively sirolimus-analogue active drugs, and stent backbones with thin struts (50–100 μm) composed of stainless steel, cobalt chromium, or platinum chromium.[572–577] New-generation DES have higher efficacy and safety in comparison with both early-generation DES and BMS.[336,571,578] Although stenting with new-generation DES confers a similar risk of death or MI at mid- to long-term follow-up in comparison with BMS,[579] the risk of subacute and late stent thrombosis is significantly lower.[579,580] Moreover, the risk of very late stent thrombosis is at least comparable to that of BMS and lower than that of early-generation DES.[336,571,579,580] These observations were confirmed in a recent trial enrolling patients aged 75 years or older and demonstrating superior outcomes (composite of all-cause mortality, MI, stroke, or ischaemia-driven target lesion revascularization) with DES as compared with BMS with similar duration of intended DAPT (1 month or 6 months) in both treatment arms.[581] Similarly, there is no clear evidence of a difference between DES and BMS on the risk of stent thrombosis following unplanned disruption of DAPT.[565] Accordingly, new-generation DES should be preferred to BMS for routine use.

A large number of new-generation DES have received approval for use and CE mark in Europe.[578] Supplementary *Table 6* displays a list of new-generation DES with the CE mark and evidence from large-scale clinical trials powered for clinical primary endpoints.

Biodegradable polymer and polymer-free DES offer the potential to reduce late adverse events after PCI by eliminating inflammatory reactions to permanent polymer coatings. A number of large-scale trials showed comparable efficacy and safety compared with permanent polymer stents.[575,576,582–590] However, at the moment, there is no evidence of differential efficacy with new-generation biodegradable polymer DES in comparison with new-generation permanent polymer DES in large-scale randomized trials with follow-up out to 5 years.[591–594]

Regarding polymer-free DES, two large-scale trials with different devices showed comparable results with new-generation DES and superior results to BMS.[173,577] Long-term follow-up from randomized trials vs. new-generation permanent polymer DES is only available for a single device and shows comparable outcomes between the devices.[591]

The high clinical efficacy and safety of new-generation DES support their preferred use in patients with an indication for PCI, including patients with diabetes, CKD, multivessel and LMS disease, AMI, vein grafts, restenotic lesions, and chronic total occlusions. New-generation DES should therefore be considered as the default stent type for PCI regardless of clinical presentation, lesion subtype, concomitant therapies, or comorbidities.

16.1.3 Bioresorbable scaffolds

Completely bioresorbable scaffolds (BRS), which degrade to predominantly inert end products after fulfilling their scaffold function in the lesion site of the coronary vessel, have been developed with the goal of reducing or eliminating stent-related adverse events at long-term follow-up. Current scaffold platforms to have reached clinical testing are based on two different technologies: bioresorbable, polymer-based scaffolds (resorption up to 3–4 years) and resorbable, metallic (magnesium) scaffolds (resorption up to 1 year).[595] Although a number of devices have received approval for use in Europe (see Supplementary *Table 7*), randomized trial data are available only with the Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular).

The safety and efficacy profile of the Absorb BVS has been compared with contemporary DES in several trials. Findings of these trials as well as meta-analyses consistently indicate the inferior efficacy and safety of Absorb BVS compared with contemporary DES during long-term follow-up. Specifically, the Absorb BVS is associated with a significantly increased risk of target lesion revascularization and device thrombosis, with numbers needed to harm of 40–60.[596,597] Of note, commercial use of the Absorb BVS was stopped in 2017 (for additional details see the Supplementary Data).

Available evidence on the magnesium scaffold is limited to small observational studies. Initial results appear encouraging, but further evaluation is needed. Therefore, the Task Force endorses the recommendation of the recent ESC/European Association for Percutaneous Cardiovascular Interventions (EAPCI) document on bioresorbable scaffolds that any BRS should not be used outside well-controlled clinical studies. In patients who have been treated with BRS, prolonged-duration DAPT for 3 years or longer may be considered.

16.1.4 Drug-coated balloons

The rationale for using DCBs is based on the concept that with highly lipophilic drugs, even short contact times between the balloon surface and the vessel wall are sufficient for effective drug delivery. There are various types of DCB that are approved for use in Europe and their main characteristics are listed in Supplementary *Table 8*. Although specifically designed comparative randomized trials are lacking, a class effect for all DCBs cannot be assumed.[598] Randomized trial data supporting the use of DCB angioplasty are limited to the treatment of in-stent restenosis (see section 13.4). In terms of the use of DCB angioplasty for *de novo* disease, a number of small randomized trials have been reported with somewhat conflicting results.[599–601] At present, there are no convincing data to support the use of DCB angioplasty for this indication.

16.1.5 Devices for lesion preparation

Lesion preparation is critical for successful PCI. In addition to plain balloon angioplasty (with standard or non-compliant balloons), cutting or scoring balloon angioplasty or rotational atherectomy may be required in selected lesions—particularly those with heavy calcification—in order to adequately dilate lesions prior to stent implantation. However, studies investigating the systematic use of these adjunctive technologies, such as rotational atherectomy, have failed to show clear clinical benefit.[602]

16.2 Invasive imaging tools for procedural guidance

16.2.1 Intravascular ultrasound

The majority of the existing clinical trial data relate to the use of IVUS guidance during PCI. In the BMS era, several RCTs addressed the potential of IVUS in reducing restenosis and adverse events after

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stenting, with somewhat conflicting results. Findings from one meta-analysis of randomized trials suggested better outcomes with IVUS guidance in terms of acute procedural results and reduced angiographic restenosis, repeat revascularization, and MACE, with no effect on death and MI.[603,604] In the DES era, meta-analysis of randomized and observational studies also suggests better clinical outcomes with IVUS-guided vs. angiography-guided PCI.[605,606] However, the contribution of findings from observational studies must be weighed against the likelihood of considerable residual confounding due to treatment selection bias. Similarly, findings of improved outcome in patients undergoing LM stem PCI with IVUS-guided PCI vs. angiography-guided PCI from a propensity score matched analysis must be interpreted with caution.[35]

In cases of stent failure, including restenosis and stent thrombosis, the use of IVUS should be considered in order to identify and correct underlying mechanical factors (see section 13).[386]

16.2.2 Optical coherence tomography

A number of studies have assessed OCT imaging for PCI guidance. Two observational studies show that while OCT imaging changes operator behaviour, its impact on clinical outcomes is unclear.[607,608] Indeed, OCT is more accurate than angiography or IVUS in detecting subtle morphological details including malapposition, residual thrombus, plaque prolapse, and residual dissections, although many of these additional findings may have a benign course.[609,610] A single randomized trial compared OCT with IVUS and coronary angiography, and showed that OCT-guided PCI was safe and resulted in a similar minimum stent area to that of IVUS-guided PCI.[611] However, OCT guidance was not superior to either IVUS or angiography alone. An additional randomized trial that enrolled patients with NSTE-ACS compared OCT-guided PCI with angiography-guided PCI and found no signal of impact on clinical outcomes.[612]

A number of observational studies have shown that OCT is feasible and safe in the assessment of stent failure due to thrombosis, and may yield information that may be clinically useful.[386,387,613,614] Likewise, in cases of in-stent restenosis, intrastent neointimal tissue may be characterized by OCT, enabling for example the detection of neoatherosclerosis.[386,615,616] In cases of stent failure, the use of OCT should be considered in order to identify and correct underlying mechanical factors (see section 13).

16.3 Specific lesion subsets

16.3.1 Bifurcation stenosis

A number of RCTs have investigated the optimal intervention strategy in patients with bifurcation lesions and showed no benefit for the systematic two-stent approach vs. main branch-only stenting with provisional stenting of the side branch in terms of clinical outcomes.[617] A recent pooled analysis of two RCTs showed lower 5 year survival in patients randomized to a systematic two-stent approach.[618] In addition, procedure time, contrast volume, radiation exposure, and cost are higher with a two-stent approach.[618] The EBC TWO (European Bifurcation Coronary TWO) trial found no difference between a provisional T-stent strategy and a systematic two-stent strategy (culotte technique) in terms of the composite endpoint of death, MI, and TVR at 12 months among 200 patients with large-calibre true bifurcation lesions (side branch diameter ≥2.5 mm) and significant ostial disease length (≥5 mm).[619] Thus, main branch-only stenting with provisional stenting of the side branch should be the preferred approach for most bifurcation lesions. Exceptions to this rule, where upfront side branch stenting may be preferable, include the presence of a large side branch (≥2.75 mm) with a long ostial side branch lesion (>5 mm) or anticipated difficulty in accessing an important side branch after main branch stenting, and true distal LM bifurcations. Recently, a multicentre trial conducted in China directly compared a double-kissing crush two-stent strategy with provisional stenting of the main branch in 482 patients with distal LM bifurcation disease. Double-kissing crush resulted in a lower risk of the primary endpoint target lesion failure at 1 year compared with provisional stenting.[620]

When a two-stent strategy is necessary, which two-stent technique should be preferred is debated. The three most widely used contemporary two-stent techniques are culotte, crush (classic or double-kissing crush), and T and protrusion (TAP).[621,622] Several RCTs have compared these techniques. In non-LM bifurcation lesions, there is no compelling evidence that one technique is superior to the others in terms of major clinical endpoints.[621,622] In LM true bifurcation lesions, double-kissing crush has the most favourable outcome data.[623]

Final 'kissing' balloon dilation is generally recommended when two stents are eventually required, with no advantage from final kissing with the one-stent technique.[624,625] Several stents, designed specifically for the treatment of bifurcation lesions, have undergone extensive evaluation with promising angiographic and clinical results, though RCTs against current recommended therapy are limited.[626] Further technical details relating to bifurcation PCI are described in the consensus document of the European Bifurcation Club.[627]

16.3.2 Chronic total coronary occlusion

Dedicated RCTs examining the outcomes of patients with chronic total occlusion (CTO) allocated to revascularization or conservative therapy are scarce. One trial randomized patients with STEMI and CTO in a non-culprit vessel to CTO-PCI vs. conservative therapy, and found no difference in the primary endpoint of LVEF and LV end-diastolic volume at 4 months.[628] More recently, the prospective randomized EUROCTO (Randomized Multicentre Trial to Compare Revascularization With Optimal Medical Therapy for the Treatment of Chronic Total Occlusions) trial showed symptomatic improvement by PCI of CTO.[629] This trial included 396 patients who were randomly assigned to PCI of CTO with optimal medical therapy, or optimal medical therapy alone. During the 12 month follow-up, the primary endpoint-the change in health status assessed by the Seattle angina questionnaire-showed significantly greater improvement of angina frequency and quality of life with CTO PCI as compared with optimal medical therapy alone. Yet, MACE were comparable between the two groups. A systematic review of 25 observational studies showed that at median follow-up of 3 years, successful CTO-PCI was associated with improved clinical outcomes in comparison with failed revascularization, including overall survival, angina burden, and the requirement for bypass surgery.[630] Broadly speaking, the treatment of CTOs may be considered analogous to the treatment of non-CTO lesions (see recommendations in section 5). In cases of regional wall motion abnormalities in the territory of the CTO, objective evidence of viability should be sought. The decision to attempt CTO-PCI should be considered against the risk of greater contrast volume, longer fluoroscopy time, and higher MACE rates in comparison with non-CTO PCI patients.[631] *Ad hoc* PCI is generally not recommended for CTOs, although it may be necessary in selected cases (e.g. acute bypass graft failure not amenable to recanalization of the bypass graft).

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Recent developments in catheter and wire technology, and increasing operator expertise with both antegrade and retrograde approaches as well as wire escalation and dissection/re-entry techniques, have translated into increasing success rates of CTO-PCI with low rates of MACE.[631–633] Success rates are strongly dependent on operator skills, depending on experience with specific procedural techniques, and the availability of dedicated equipment, and vary from 60–70% to >90%.[631–633]

16.3.3 Ostial lesions

In ostial coronary lesions, additional judgement and caution is essential before proceeding to PCI. In particular, a catheter-induced coronary spasm must be rigorously excluded. Lesion assessment with IVUS may be helpful, particularly in LM ostial stenosis. FFR measurement may also be valuable in the assessment of ostial lesions of borderline significance,[634] taking special care to avoid a wedge position of the guiding catheter and using i.v., rather than intracoronary, adenosine. When performing an intervention, due to interaction between the guide catheter and the proximal stent edge, the risk of longitudinal stent deformation must be considered[635] and avoided with careful catheter manipulation. The accurate positioning of the stent, precisely in the coronary ostium, may be technically challenging and some specialized techniques that may help to achieve optimal stent placement have been described.[636,637]

16.4 Vascular access

A number of RCTs have compared radial access with femoral access for diagnostic angiography and PCI. The two largest were RIVAL (Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes) and MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial access Site and Systemic Implementation of AngioX).[172,638] In the RIVAL trial, which enrolled 7021 patients, the primary outcome of death, MI, stroke, or non-CABG-related major bleeding at 30 days occurred at a similar rate in radial vs. femoral access (HR 0.92, 95% CI 0.72–1.17, P = 0.50).[638] In the MATRIX trial, 8404 ACS patients were randomly allocated to radial or femoral access.[172] In terms of the first co-primary endpoint of 30 day MACE, there was no significant difference between radial access and femoral access (RR 0.85, 95% CI 0.74–0.99, two-sided P = 0.031; non-significant at a pre-specified α of 0.025). The second co-primary outcome of 30 day net adverse clinical events [MACE or non-CABG BARC (Bleeding Academic Research Consortium (major bleeding] was significantly lower with radial access (RR 0.83, 95% CI 0.73–0.96; P = 0.009). Major BARC 3 or 5 bleeding was significantly reduced in the radial group (1.6 vs. 2.3%; RR 0.67, 95% CI 0.49–0.92; P = 0.013), and radial access was associated with a lower risk of all-cause mortality (1.6 vs. 2.2%; RR 0.72, 95% CI 0.53–0.99, P = 0.045). However, the benefit of radial over femoral access depends upon the operator's expertise in the radial technique.[639]

Treatment of restenotic and saphenous vein graft lesions are discussed in section 13.3.

Recommendations on choice of stent and access site

Recommendations	Class[a]	Level[b]
DES are recommended over BMS for any PCI irrespective of: • clinical presentation • lesion type • planned non-cardiac surgery • anticipated duration of DAPT • concomitant anticoagulant therapy.[100,578,579,640]	I	A
Radial access is recommended as the standard approach, unless there are overriding procedural considerations.[172,638,641]	I	A
BRS are currently not recommended for clinical use outside of clinical studies.[642–650]	III	C

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BMS = bare-metal stents; BRS = bioresorbable scaffolds; DAPT = dual antiplatelet therapy; DES = drug-eluting stents; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations on intravascular imaging for procedural optimization

Recommendations	Class[a]	Level[b]
IVUS or OCT should be considered in selected patients to optimize stent implantation.[603,612,651–653]	IIa	B
IVUS should be considered to optimize treatment of unprotected left main lesions.[35]	IIa	B

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IVUS = intravascular ultrasound; OCT = optical coherence tomography.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations on specific lesion subsets

Recommendations	Class[a]	Level[b]
Stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch, is recommended for PCI of bifurcation lesions.[654–658]	I	A
Percutaneous revascularization of CTOs should be considered in patients with angina resistant to medical therapy or with a large area of documented ischaemia in the territory of the occluded vessel.[629,659–663]	IIa	B
In true bifurcation lesions of the left main, the double-kissing crush technique may be preferred over provisional T-stenting.[620]	IIb	B

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CTO = chronic total occlusion; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

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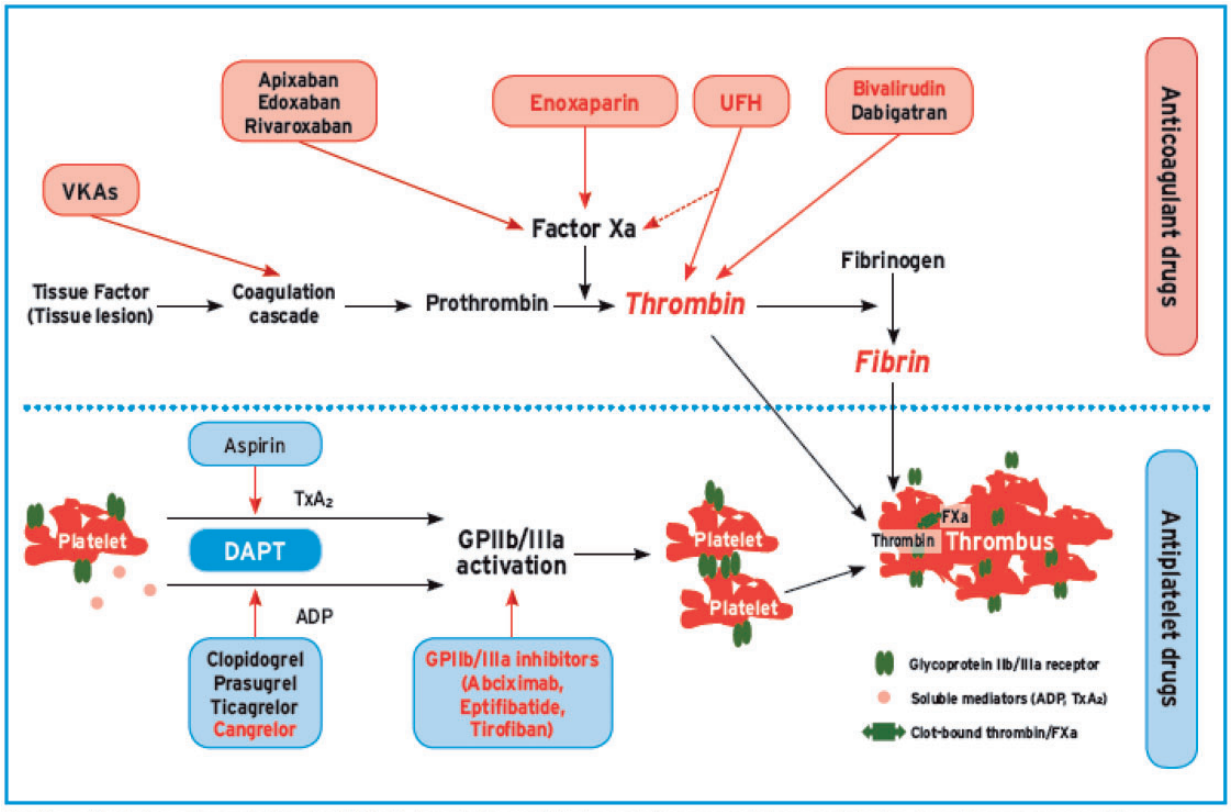
17 Antithrombotic treatments

Antithrombotic treatment is mandatory in CAD patients undergoing myocardial revascularization. The choice of treatment, the combination, the time point of initiation, and the duration depend on the patient's characteristics, comorbidities, the clinical setting (elective revascularization vs. ACS), and the mode (PCI vs. CABG) of revascularization. Both ischaemic and bleeding events significantly influence the outcome of CAD patients and their overall mortality risk during and after myocardial revascularization.[664] Thus, the choice of treatment should reflect the ischaemic and bleeding risk. The recommended drugs (*Figure 9*) and doses (*Table 7*) for anticoagulant and antiplatelet drugs used in conjunction with myocardial revascularization are summarized below.



The figure illustrates anticoagulant and antiplatelet drugs being used during and after myocardial revascularization (percutaneous coronary intervention or coronary artery bypass grafting). Drugs with oral administration are shown in black letters and drugs with preferred parenteral administration in red.
ADP = adenosine diphosphate; DAPT = dual antiplatelet therapy; FXa = factor Xa; GP = glycoprotein; TxA_2 = thromboxane A_2; UFH = unfractionated heparin; VKAs = vitamin K antagonists.

Figure 9 Antithrombotic treatment for myocardial revascularization and its pharmacological targets.

Table 7 Doses of antiplatelet and anticoagulant drugs used during and after myocardial revascularization

Antiplatelet drugs	
Aspirin	Loading dose of 150–300 mg orally or 75–150 mg i.v. if oral ingestion is not possible, followed by a maintenance dose of 75–100 mg/day.
Clopidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of 75 mg/day.
Prasugrel	Loading dose of 60 mg orally, followed by a maintenance dose of 10 mg/day. In patients with body weight <60 kg, a maintenance dose of 5 mg is recommended. In patients aged >75 years, prasugrel is generally not recommended, but a dose of 5 mg should be used if treatment is deemed necessary.

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Ticagrelor	Loading dose of 180 mg orally, followed by a maintenance dose of 90 mg b.i.d.
Abciximab	Bolus of 0.25 mg/kg i.v. and 0.125 μg/kg/min infusion (maximum 10 μg/min) for 12 h.
Eptifibatide	Double bolus of 180 μg/kg i.v. (given at a 10 min interval) followed by an infusion of 2.0 μg/kg/min for up to18 h.
Tirofiban	Bolus of 25 μg/kg over 3 min i.v., followed by an infusion of 0.15 μg/kg/min for up to 18 h.
Cangrelor	Bolus of 30 μg/kg i.v. followed by 4 μg/kg/min infusion for at least 2 h or duration of procedure, whichever is longer.
Anticoagulant drugs for PCI	
Unfractionated heparin	• 70–100 U/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned. • 50–70 U/kg i.v. bolus with GP IIb/IIIa inhibitors.
Enoxaparin	0.5 mg/kg i.v. bolus.
Bivalirudin	0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/h for up to 4 h after the procedure as clinically warranted.
Oral anticoagulant drugs (concomitant treatment after PCI)	
Vitamin K antagonists (e.g. warfarin, phenprocoumon)	Dosing is based on INR value and the respective clinical indication.
Apixaban	Maintenance doses of 5 and 2.5[a] mg b.i.d.
Dabigatran	Maintenance doses of 150 and 110 mg b.i.d.
Edoxaban	Maintenance doses of 60 and 30[a] mg/day
Rivaroxaban	Maintenance doses of 20 and 15[a] mg/day, and 2.5 mg b.i.d. (vascular dose).

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[a]Specific criteria for reduced dose apply (see recommendation table on page 61).
b.i.d. = twice daily; GP = glycoprotein; INR = international normalized ratio; i.v. = intravenous; PCI = percutaneous coronary intervention.

17.1 Percutaneous coronary intervention in stable coronary artery disease

17.1.1 Choice of treatment and pre-treatment

DAPT consisting of aspirin and a $P2Y_{12}$ receptor inhibitor represents the cornerstone of treatment in patients undergoing elective PCI.[665] The $P2Y_{12}$ receptor inhibitor clopidogrel is recommended for elective stenting procedures. For routine clopidogrel pre-treatment (administration of the drug when the coronary anatomy is unknown), there is no compelling evidence for a significant clinical benefit in SCAD patients.[666–668] Thus, pre-treatment may only be an option in selected patients with high probability of PCI or before staged PCI procedures. *Figures 9 and 10* summarize the commonly used antiplatelet and anticoagulant drugs in SCAD patients undergoing PCI.

17.1.2 Peri-interventional treatment

While aspirin and clopidogrel are indicated for elective stenting procedures, prasugrel or ticagrelor may only be considered in selected patients for specific high-risk situations of elective stenting (e.g. complex PCI procedures such as LM stenting and CTO procedures) or in patients with a history of stent thrombosis on clopidogrel treatment.

In parallel with antiplatelet treatment, the use of anticoagulants is standard of care during elective PCI to inhibit thrombin generation and activity. Different agents, including unfractionated heparin (UFH) and bivalirudin, have been evaluated for their use in clinical practice. The REPLACE-2 (Randomised Evaluation in PCI Linking Angiomax to Reduced Clinical Events 2) trial demonstrated that the outcome with bivalirudin and provisional glycoprotein (GP) IIb/IIIa blockade is similar to that of UFH plus planned GP IIb/IIIa inhibition during elective PCI.[669] The ISAR-REACT (Intracoronary Stenting and Antithrombotic Regimen Rapid Early Action for Coronary Treatment) 3 trial also showed a similar outcome for bivalirudin vs. UFH treatment.[670] In ISAR REACT 3A,[671] evaluating a lower dose of 100 U/kg UFH, this lower dose showed net clinical benefit compared with the historical control cohort and this benefit was mostly driven by a reduction in bleeding events. In view of the primary endpoint results of the RCTs and in view of a trend towards a lower risk of MI, UFH remains the standard anticoagulant for elective PCI. Based on the results of the STEEPLE (Safety and Efficacy of Intravenous Enoxaparin in Elective Percutaneous Coronary Intervention Randomised Evaluation) trial, enoxaparin should be considered as an alternative anticoagulant drug.[672]

Drugs for parenteral antiplatelet treatment include cangrelor and GP IIb/IIIa inhibitors. Cangrelor is a direct reversible, short-acting $P2Y_{12}$-inhibitor that has been evaluated during PCI for SCAD and ACS in clinical trials comparing cangrelor with clopidogrel, administered before PCI [CHAMPION (Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet

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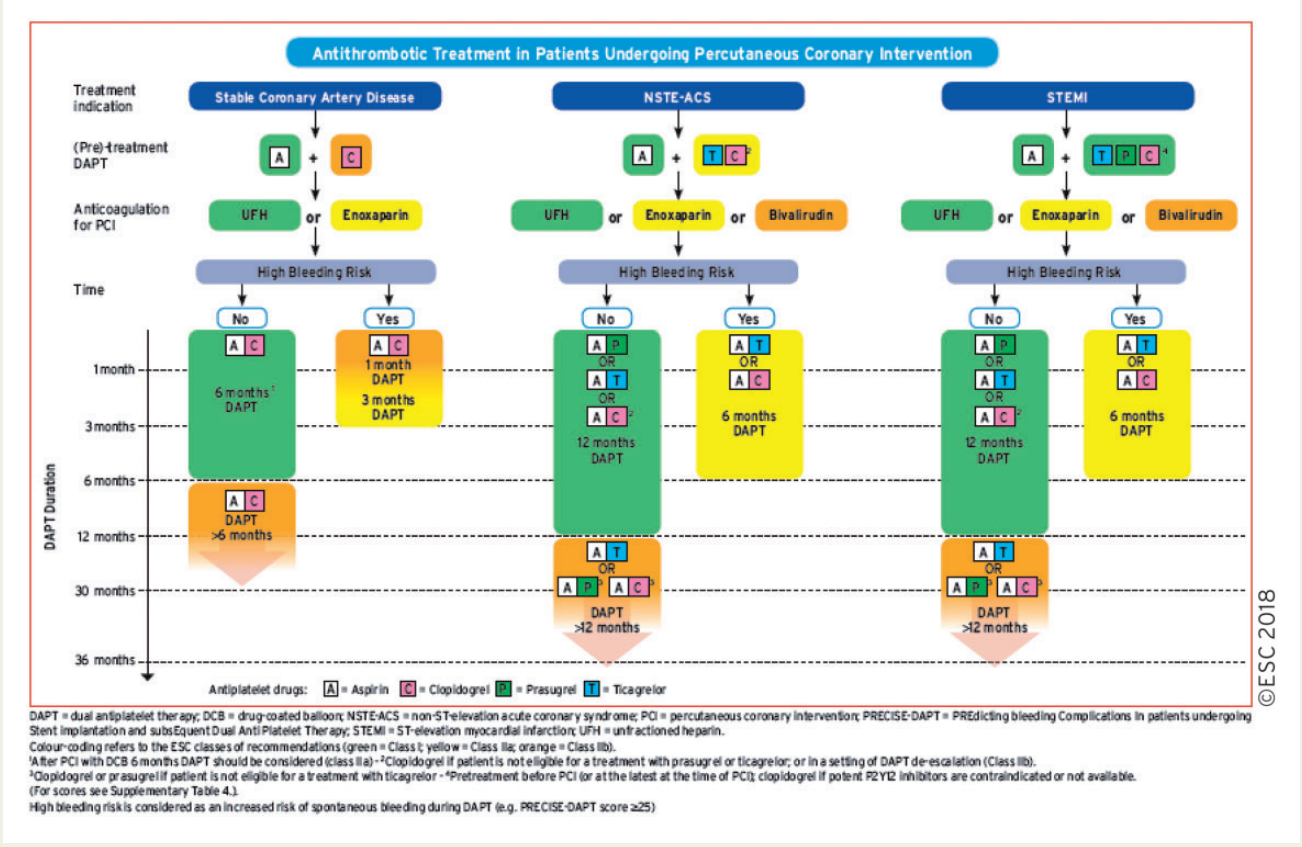
Inhibition) PCI] or after PCI (CHAMPION PLATFORM and CHAMPION PHOENIX).[673] A meta-analysis showed a benefit with respect to major ischaemic endpoints that is counterbalanced by an increase in relevant bleeding.[673] Moreover, the benefit of cangrelor with respect to ischaemic endpoints was attenuated in CHAMPION PCI with upfront administration of clopidogrel. Nevertheless, due to its proven efficacy in preventing intraprocedural and post-procedural stent thrombosis in $P2Y_{12}$-inhibitor naïve patients, cangrelor may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI (for more detailed discussion see the Supplementary Data).

Available GP IIb/IIIa inhibitors include abciximab, eptifibatide, and tirofiban. In a setting of elective PCI, clinical trials did not demonstrate an additional benefit of GP IIb/IIIa inhibitor administration in SCAD patients in a setting of DAPT treatment that includes loading with clopidogrel.[674,675] A meta-analysis on this topic revealed no mortality benefit of GP IIb/IIIa treatment and while non-fatal MIs were reduced, (minor) bleeding events were significantly higher when utilizing these agents.[676] Thus, GP IIb/IIIa inhibitors may only be considered in specific 'bail-out' situations including high intraprocedural thrombus burden, slow flow, or no-flow with closure of the stented coronary vessel.

An algorithm for the use of antithrombotic drugs in patients undergoing PCI is shown in *Figure 10*.

17.1.3 Post-interventional and maintenance treatment

Following elective stenting, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type. In specific clinical scenarios, this standard DAPT duration can be shortened (<6 months) or extended (>6–12 months). For a more detailed description of the pertinent clinical trials in the field of DAPT duration, we refer the reader to the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[410] Following DAPT, a life-long single antiplatelet therapy (usually with aspirin) is recommended, and patients should be advised not to prematurely discontinue oral antiplatelet therapy after stenting due to the risks of stent thrombosis and recurrent MI.[677] Recently, the value of a vascular dose of rivaroxaban (2.5 mg b.i.d.) in conjunction with aspirin was demonstrated in the large-scale COMPASS (Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease) trial.[678] However, its utilization in SCAD patients is a matter of secondary prevention and is not linked to myocardial revascularization procedures.



DAPT = dual antiplatelet therapy; DCB = drug-coated balloon; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications in patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; STEMI = ST-elevation myocardial infarction; UFH = unfractioned heparin.
Colour-coding refers to the ESC classes of recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).
[1]After PCI with DCB 6 months DAPT should be considered (class IIa) - [2]Clopidogrel if patient is not eligible for a treatment with prasugrel or ticagrelor; or in a setting of DAPT de-escalation (Class IIb).
[3]Clopidogrel or prasugrel if patient is not eligible for a treatment with ticagrelor - [4]Pretreatment before PCI (or at the latest at the time of PCI); clopidogrel if potent P2Y12 inhibitors are contraindicated or not available.
(For scores see Supplementary Table 4.).
High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥25)

Figure 10 Algorithm for the use of antithrombotic drugs in patients undergoing percutaneous coronary intervention. High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score ≥25). Colour-coding refers to the ESC classes of recommendations (green = class I; yellow = class IIa; and orange = class IIb).

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Recommendations for antithrombotic treatment in stable coronary artery disease patients undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Pre-treatment and antiplatelet therapy		
Treatment with 600 mg clopidogrel is recommended in elective PCI patients once the coronary anatomy is known and a decision is made to proceed with PCI.[667,679,680]	I	A
Pre-treatment with clopidogrel may be considered if the probability of PCI is high.	IIb	C
In patients on a maintenance dose of 75 mg clopidogrel, a new loading dose of 600 mg may be considered once the indication for PCI is confirmed.	IIb	C
Peri-interventional treatment		
Aspirin is indicated before elective stenting.[681–683]	I	A
An oral loading dose of aspirin (150–300 mg p.o. or 75–250 mg i.v.) is recommended if the patient is not pre-treated.	I	C
Clopidogrel (600 mg loading dose, 75 mg daily maintenance dose) is recommended for elective stenting.[684–688]	I	A
Glycoprotein IIb/IIIa antagonists should be considered only for bail-out.	IIa	C
Prasugrel or ticagrelor may be considered in specific high-risk situations of elective stenting (e.g. history of stent thrombosis or left main stenting).	IIb	C
Unfractionated heparin is indicated as the standard anticoagulant (70–100 U/kg).[670,671]	I	B
Bivalirudin (0.75 mg/kg bolus, followed by 1.75 mg/kg/h for up to 4 h after the procedure) is indicated in the case of heparin-induced thrombocytopenia.	I	C
Enoxaparin (i.v. 0.5 mg/kg) should be considered as an alternative agent.[672,689]	IIa	B
Cangrelor may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI.[673]	IIb	A
Post-interventional and maintenance treatment		
Life-long single antiplatelet therapy, usually aspirin, is recommended.[681,683]	I	A
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C
In patients with SCAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type.[c] [690–694]	I	A
In patients with SCAD treated with BRS, DAPT should be considered for at least 12 months and up to the presumed full absorption of the BRS, based on an individual assessment of bleeding and ischaemic risk.	IIa	C
In patients with SCAD treated with DCB, DAPT should be considered for 6 months.[369,371]	IIa	B
In patients with SCAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥25), DAPT should be considered for 3 months.[d] [695,696]	IIa	A
In patients with SCAD who have tolerated DAPT without a bleeding complication and who are at low bleeding risk but high thrombotic risk, continuation of DAPT with clopidogrel for >6 months and up to 30 months may be considered.[697–700]	IIb	A
In patients with SCAD in whom 3 month DAPT poses safety concerns, DAPT may be considered for 1 month.	IIb	C

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BRS = bioresorbable scaffold; CAD = coronary artery disease; DAPT = dual antiplatelet therapy; DCB = drug-coated balloon; i.v. = intravenous; MI = myocardial infarction; PCI = percutaneous coronary intervention; p.o. = orally; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; SCAD = stable coronary artery disease.

[a]Class of recommendation.

[b]Level of evidence.

[c]These recommendations refer to stents that are supported by large-scale randomized trials with clinical endpoint evaluation leading to an unconditional CE mark.

[d]The evidence supporting this recommendation comes from two studies where the zotarolimus-eluting Endeavour stent was investigated in conjunction with a 3 month DAPT regimen.

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17.2 Non-ST-segment elevation acute coronary syndrome

The activation of blood platelets and the coagulation cascade plays a key role in the initial phase and evolution of an ACS. Hence, sufficient platelet inhibition and anticoagulation is essential during ACS, and especially in ACS patients undergoing PCI.

17.2.1 Choice of treatment and pre-treatment

For NSTE-ACS patients, DAPT including aspirin and a potent $P2Y_{12}$ receptor inhibitor (prasugrel or ticagrelor) is recommended (see the Supplementary Data).[701,702] Clopidogrel should only be used when prasugrel or ticagrelor are not available or are contraindicated. Based on the results of the ACCOAST (Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention or as Pretreatment at the Time of Diagnosis in Patients with Non-ST Elevation Myocardial Infarction) trial,[165] it is not recommended that prasugrel is administered in patients in whom coronary anatomy is not known. Nevertheless, pre-treatment with ticagrelor was part of the PLATO trial (Study of Platelet Inhibition and Patient Outcomes) and was associated with an early benefit over clopidogrel.[702] For these reasons, pre-treatment with ticagrelor can be used, although there is no direct evidence from head-to-head comparisons between pre-treatment strategies.

17.2.2 Peri-interventional treatment

Anticoagulation is recommended for all patients in addition to antiplatelet therapy during PCI for NSTE-ACS.[703] In general, a crossover between anticoagulants should be avoided [especially between UFH and low-molecular-weight heparin (LMWH)], with the exception of adding UFH to fondaparinux when a patient proceeds to PCI.[704,705] The respective agents should be discontinued after PCI except for specific clinical settings, such as the presence of an LV aneurysm with thrombus or AF requiring anticoagulation.

A number of trials have compared bivalirudin with UFH in ACS patients undergoing PCI (see the Supplementary Data). Some of these trials pursued a balanced use of adjunctive GP IIb/IIIa inhibitors with both bivalirudin and heparin, whereas others, predominantly the older ones, had selective use of GP IIb/IIIa inhibitors in the heparin arm. These trials have been reviewed extensively in a number of meta-analyses.[706–708] A meta-analysis that included the MATRIX trial but not VALIDATE-SWEDEHEART (Bivalirudin versus Heparin in ST-Segment and Non-ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy on the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) showed no significant benefit of bivalirudin compared with UFH with respect to death, MACE, and MI.[708] Nevertheless, bivalirudin was associated with a significant increase in the risk of stent thrombosis and a significant decrease in the risk of bleeding. However, the reduction of bleeding risk was linked to unbalanced use of GP IIb/IIa inhibitors predominantly with UFH. Recently, the VALIDATE-SWEDEHEART study[709] compared UFH vs. bivalirudin in a background of radial access and limited use of GP IIb/IIIa inhibitors. The study demonstrated similar risk patterns for both ischaemia and bleeding when comparing the two drugs. Of note, while prior studies reported a reduced bleeding risk with bivalirudin vs. UFH, this was not confirmed in VALIDATE-SWEDEHEART and in a contemporary setting of preferred radial access and selective use of GP IIb/IIIa inhibitors. More recently, a meta-analysis updated for the results of VALIDATE-SWEDEHEART confirmed that bivalirudin compared with heparin was associated with a similar incidence of all-cause death and ischaemic events after PCI for ACS.[710] A significant association of bivalirudin with decreased risk of bleeding was only found with unbalanced use of GP IIb/IIIa inhibitors in conjunction with heparin. In summary and based on the above-mentioned trials, UFH is primarily recommended as an anticoagulant for PCI. Due to its short half-life and favourable results in some of the studies, bivalirudin may be considered as an alternative to UFH in selected cases.

Patients may undergo cardiac catheterization after a conservative treatment phase and these patients are commonly treated with fondaparinux during the conservative treatment phase. This regimen is based on the OASIS-5 (Optimal Antiplatelet Strategy for Interventions 5) trial.[711] Of note, catheter thrombus formation was an issue with fondaparinux and therefore full-dose UFH must be added to prevent thrombus formation when the patient proceeds to PCI. Enoxaparin should be considered as anticoagulant for PCI in patients pre-treated with subcutaneous enoxaparin. A benefit of enoxaparin over UFH in reducing mortality and bleeding complications was recently reported in a meta-analysis including NSTE-ACS patients.[689] Yet, this meta-analysis did not include a dedicated randomized study in NSTE-ACS and was largely based on non-randomized comparisons.

Most of the trials evaluating GP IIb/IIIa inhibitors in PCI-treated patients pre-date the era of routine oral DAPT treatment. These early trials demonstrated a reduction in the incidence of ischaemic events in favour of GP IIb/IIIa treatment in combination with UFH compared with UFH alone, primarily through a reduction in MI.[712] However, coronary angiography and PCI were delayed compared with what is recommended now, and a consistent major bleeding risk was observed. Overall, there is no compelling evidence for an additional benefit of routine upstream use of GP IIb/IIIa inhibitors in NSTE-ACS patients scheduled for coronary angiography and receiving DAPT treatment.[713,714] In a setting of potent platelet inhibition with ticagrelor or prasugrel, where randomized data on GP IIb/IIIa inhibitor use is limited, routine use of these agents cannot be recommended. Nevertheless, it should be considered for bail-out situations or thrombotic complications, and may be used for high-risk PCI in patients without pre-treatment with $P2Y_{12}$-inhibitors. The available evidence on cangrelor suggests that the potential benefit is independent of the clinical presentation. Thus, similar to SCAD patients, cangrelor may be considered in specific settings in $P2Y_{12}$-naïve patients undergoing PCI.

17.2.3 Post-interventional and maintenance treatment

Following PCI for NSTE-ACS, DAPT consisting of a $P2Y_{12}$ receptor inhibitor in addition to aspirin is generally recommended for 12 months, irrespective of the stent type. Recently, the SMART-DATE (Smart Angioplasty Research Team-safety of 6-month duration of Dual Antiplatelet Therapy after percutaneous coronary intervention in patients with acute coronary syndromes) prospective multicentre randomized trial supported this notion in the setting of contemporary interventional practice. The study randomly assigned 2712

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patients undergoing PCI for NSTE-ACS or STEMI to either 6 month DAPT or 12 month or longer DAPT. Although the primary endpoint—a composite of all-cause death, MI, or stroke—did not confirm the benefit of prolonged DAPT over 6 month DAPT (cumulative event rate 4.7 vs. 4.2%; absolute risk difference 0.5%; upper limit of one-sided 95% CI 1.8%; $P_{\text{non-inferiority}} = 0.03$ with a predefined non-inferiority margin of 2.0%), MI occurred more frequently in the 6 month DAPT group than in the prolonged DAPT group (1.8 vs. 0.8%; $P = 0.02$). The rate of BARC type 2 - 5 bleeding was not significantly affected by prolonged DAPT (HR 0.69, 95% CI 0.45–1.05, $P = 0.09$). The authors stated that the increased risk of MI with 6 month DAPT and the wide non-inferiority margin prevented them from concluding that short-term DAPT was safe in this setting, and suggested that prolonged DAPT should remain the standard of care in patients with ACS without excessive risk of bleeding.[715]

In specific clinical scenarios, this standard DAPT duration can be shortened (<12 months) or extended (>12 months). Further on, switching and especially a de-escalation of DAPT (switching from potent $P2Y_{12}$-inhibitors to clopidogrel) was subject to a number of randomized clinical trials.[716,717] Triggers for DAPT de-escalation include clinical (bleeding events or presumed high bleeding risk) and socio-economic factors.[716] Based on recent results from the randomized TROPICAL-ACS (Testing responsiveness to platelet inhibition on chronic antiplatelet treatment for acute coronary syndromes) trial[717], an approach of DAPT de-escalation guided by platelet function testing may be considered in ACS patients (NSTE-ACS and STEMI) as an alternative to 12 months potent platelet inhibition, especially for patients deemed unsuitable for maintained potent platelet inhibition. For a more detailed description of the pertinent clinical trials in the field of DAPT duration and switching antiplatelet drugs, we refer the reader to the International Expert Consensus document on Switching Platelet P2Y12 Receptor-Inhibiting Therapies[718] and the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[410] Following DAPT, lifelong single antiplatelet therapy (usually with aspirin) is recommended and patients should be advised not to prematurely discontinue oral antiplatelet therapy after stenting.[677,719]

Based on the results of the ATLAS-ACS 2–TIMI 51 (Anti-Xa Therapy to Lower cardiovascular events in Addition to Standard therapy in subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction 51) trial in NSTE-ACS and STEMI patients,[720] low-dose rivaroxaban may be considered after discontinuation of parenteral anticoagulation for patients with no prior stroke/TIA, and at high ischaemic risk as well as low bleeding risk, receiving aspirin and clopidogrel. Of note, rivaroxaban has not been investigated in a background of potent $P2Y_{12}$-inhibitors.

Recommendations for antithrombotic treatment in patients with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Pre-treatment and antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term.[681,683,721]	I	A
A $P2Y_{12}$ inhibitor is recommended in addition to aspirin, maintained over 12 months unless there are contraindications such as an excessive risk of bleeding.[701,702,722,723] Options are:	I	A
• Prasugrel in $P2Y_{12}$-inhibitor naïve patients who proceed to PCI (60 mg loading dose, 10 mg daily dose).[701]	I	B
• Ticagrelor irrespective of the preceding $P2Y_{12}$ inhibitor regimen (180 mg loading dose, 90 mg b.i.d.).[702]	I	B
• Clopidogrel (600 mg loading dose, 75 mg daily dose) only when prasugrel or ticagrelor are not available or are contraindicated.[722–724]	I	B
GP IIb/IIIa antagonists should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C
For pre-treatment in patients with NSTE-ACS undergoing invasive management, ticagrelor administration (180 mg loading dose, 90 mg b.i.d.), or clopidogrel (600 mg loading dose, 75 mg daily dose) if ticagrelor is not an option, should be considered as soon as the diagnosis is established.	IIa	C
Cangrelor may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI.[673]	IIb	A
GP IIb/IIIa antagonists may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI.	IIb	C
Pre-treatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended.[713,714,725]	III	A
Administration of prasugrel in patients in whom coronary anatomy is not known is not recommended.[165]	III	B

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Peri-interventional therapy		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy.[703,726]	I	A
It is recommended that anticoagulation is selected according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent.	I	C
UFH is recommended.	I	C
In patients on fondaparinux, a single bolus UFH (85 IU/kg, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) is indicated.[727]	I	B
Enoxaparin should be considered in patients pre-treated with subcutaneous enoxaparin.[689]	IIa	B
Discontinuation of parenteral anticoagulation should be considered immediately after an invasive procedure.	IIa	C
Bivalirudin (0.75 mg/kg bolus, followed by 1.75 mg/kg/h for up to 4 h after the procedure) may be considered as an alternative to UFH.[163,708,710,714,728]	IIb	A
Crossover of UFH and LMWH is not recommended.[705]	III	B

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b.i.d. = twice daily; GP = glycoprotein; i.v. = intravenous; LMWH = low-molecular-weight heparin; NSTE-ACS = non-ST-segment elevation acute coronary syndromes; PCI = percutaneous coronary intervention; UFH = unfractionated heparin.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations for post-interventional and maintenance treatment in patients with non-ST-elevation acute coronary syndromes and ST-elevation myocardial infarction undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as an excessive risk of bleeding (e.g. PRECISE-DAPT ≥25).[701,702,722,723]	I	A
In patients with ACS and stent implantation who are at high risk of bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.[729,730]	IIa	B
In patients with ACS treated with BRS, DAPT should be considered for at least 12 months and up to the presumed full absorption of the BRS, based on an individual assessment of bleeding and ischaemic risk.	IIa	C
De-escalation of $P2Y_{12}$ inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) guided by platelet function testing may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition.[717]	IIb	B
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.[700,731]	IIb	A
In patients with MI and high ischaemic risk[c] who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg b.i.d. for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel.[732–734]	IIb	B
In ACS patients with no prior stroke/TIA, and at high ischaemic risk as well as low bleeding risk, receiving aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg b.i.d. for approximately 1 year) may be considered after discontinuation of parenteral anticoagulation.[720]	IIb	B

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ACS = acute coronary syndrome; b.i.d. = twice daily; BRS = bioresorbable scaffold; DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; TIA = transient ischaemic attack.
[a]Class of recommendation.
[b]Level of evidence.
[c]Defined as ≥50 years of age and having one of the following additional high-risk features: age ≥65 years or older, diabetes mellitus requiring medication, a second prior spontaneous MI, multivessel coronary artery disease, or chronic renal dysfunction, defined as an estimated creatinine clearance <60 mL/min.

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17.3 ST-segment elevation myocardial infarction

17.3.1 Choice of treatment and pre-treatment

STEMI patients undergoing primary PCI should receive aspirin and a $P2Y_{12}$ receptor inhibitor as soon as the diagnosis of STEMI is established. In line with the treatment recommendations for NSTE-ACS patients, DAPT is the cornerstone of treatment for STEMI patients and includes aspirin and a potent $P2Y_{12}$ receptor inhibitor (prasugrel or ticagrelor).[701,702] For both antiplatelet drugs, published subgroup analyses on STEMI patients are available (see the Supplementary Data). Randomized data on a comparison of ticagrelor vs. prasugrel in STEMI patients are limited, but the recently published randomized PRAGUE-18 (Comparison of Prasugrel and Ticagrelor in the Treatment of Acute Myocardial Infarction) trial[735] with limited statistical power found similar safety and efficacy profiles of ticagrelor and prasugrel in a setting of primary PCI. When potent $P2Y_{12}$ receptor inhibitors are contraindicated or are not available, clopidogrel should be given for primary PCI instead.[724] The value of pre-treatment with ticagrelor was addressed in the ATLANTIC (Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST-Elevation Myocardial Infarction to Open the Coronary Artery) trial.[736] No significant differences were observed in the levels of the two co-primary surrogate endpoints measured before PCI (thrombolysis in Myocardial Infarction flow and ST-segment resolution). Likewise, the incidence of a combined ischaemic endpoint (death, MI, stroke, stent thrombosis, and urgent revascularization) did not differ between the two treatment arms. Nevertheless, in both the TRITON (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction) and PLATO trials, pre-treatment was part of the therapeutic regimen in STEMI.

17.3.2 Peri-interventional treatment

Immediate and sufficient anticoagulation is mandatory in the setting of primary PCI for STEMI and available options include UFH, bivalirudin, and enoxaparin. A number of RCTs compared bivalirudin vs. UFH in different settings and with different utilization of GP IIb/IIIa inhibitors (see the Supplementary Data). The primary recommendation of UFH, reserving bivalirudin for selected cases, is essentially the same for primary PCI as for PCI in NSTE-ACS, and is mostly based on the same clinical trials[706,709] (see section 17.2.2).

Enoxaparin was compared with UFH in the randomized open-label ATOLL (Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischaemic and bleeding events at short- and Long-term follow-up) trial,[737] and based on the trial results, enoxaparin should be considered as an alternative to UFH treatment in STEMI patients.

A number of clinical trials, performed at a time when pre-treatment and potent platelet inhibition was not part of routine clinical practice, have documented clinical benefits of GP IIb/IIIa inhibitors as an adjunct to primary PCI performed with UFH.[738,739] A meta-analysis showed a significant survival benefit, especially in high-risk STEMI patients, but also a higher risk of bleeding with GP IIb/IIIa administration.[740] Dedicated trials have investigated the value of upstream treatment in the past.[741,742] Based upon the available evidence, the routine use of i.v. or intracoronary GP IIb/IIIa inhibitor administration—regardless of whether treatment starts upstream or in the catheterization laboratory—cannot be recommended. Especially in a setting where potent $P2Y_{12}$-inhibitors like prasugrel or ticagrelor are used, the value of GP IIb/IIIa inhibitors remains uncertain as these agents exhibit a fast onset of action (usually <1 h). GP IIb/IIIa inhibitors remain an option as bail-out therapy or in high-risk PCI without pre-treatment with $P2Y_{12}$-inhibitors. Of note, the bail-out scenarios have never been addressed in randomized controlled trials. For reasons discussed above (see sections 17.1 and 17.2), cangrelor may be considered in specific settings in $P2Y_{12}$-naïve patients undergoing PCI.

17.3.3 Post-interventional and maintenance treatment

Following PCI for STEMI, DAPT consisting of a $P2Y_{12}$ receptor inhibitor in addition to aspirin is generally recommended for 12 months. Recommendations for maintenance DAPT treatment are generally consistent with those for NSTE-ACS patients and are detailed in section 17.2.3.

Recommendations for antithrombotic treatment in ST-elevation myocardial infarction patients undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Pre-treatment and antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.[681,683,721]	I	A
A potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contraindicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.[701,702,724,743]	I	A
GP IIb/IIIa inhibitors should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI.[673]	IIb	A
GP IIb/IIIa antagonists may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI.	IIb	C

Continued

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Peri-interventional therapy		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy during PCI.[703,726]	I	A
Routine use of UFH is recommended.	I	C
Routine use of enoxaparin should be considered.[737]	IIa	B
Routine use of bivalirudin may be considered.[708,710,728,744–746]	IIb	A

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GP = glycoprotein; i.v. = intravenous; PCI = percutaneous coronary intervention; UFH = unfractionated heparin.
[a]Class of recommendation.
[b]Level of evidence.

17.4 Coronary artery bypass grafting

Antithrombotic treatment before and after CABG is addressed in the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[410] After reviewing the subsequent literature, the current Task Force endorses the recommendations of the update on DAPT and does not identify a need for any major update. Accordingly, the recommendation tables in this section are taken from the Focused Update. For a detailed discussion, we refer the reader to the Focused Update.

Dual antiplatelet therapy in patients undergoing cardiac surgery

Recommendations	Class[a]	Level[b]
It is recommended that the Heart Team estimates the individual bleeding and ischaemic risks, and guides the timing of CABG as well as the anti-thrombotic management.	I	C
In patients on aspirin who need to undergo non-emergent cardiac surgery, it is recommended to continue aspirin at a low daily regimen throughout the perioperative period.	I	C
In patients treated with DAPT after coronary stent implantation who subsequently undergo cardiac surgery, it is recommended to resume $P2Y_{12}$ inhibitor therapy post-operatively as soon as it is deemed safe, so that DAPT continues until the recommended duration of therapy is completed.	I	C
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT who are undergoing CABG and do not require long-term OAC therapy, resumption of $P2Y_{12}$ inhibitor therapy as soon as deemed safe after surgery and its continuation up to 12 months is recommended.	I	C
In patients on $P2Y_{12}$ inhibitors who need to undergo non-emergent cardiac surgery, postponing surgery for at least 3 days after discontinuation of ticagrelor, at least 5 days after clopidogrel, and at least 7 days after prasugrel should be considered.[747–749]	IIa	B
In CABG patients with prior MI who are at high risk of severe bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.	IIa	C
Platelet function testing may be considered to guide the decision on the timing of cardiac surgery in patients who have recently received $P2Y_{12}$ inhibitors.[193,750–752]	IIb	B
In patients perceived to be at high ischaemic risk with prior MI and CABG, who have tolerated DAPT without a bleeding complication, treatment with DAPT for longer than 12 months and up to 36 months may be considered.	IIb	C

Continued

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ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; DAPT = dual antiplatelet therapy; MI = myocardial infarction; NSTE-ACS = non-ST-elevation acute coronary syndrome; OAC = oral anticoagulant; STEMI = ST-elevation myocardial infarction. PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy.
[a]Class of recommendation.
[b]Level of evidence.

17.5 Special conditions

17.5.1 Antithrombotic therapy after percutaneous coronary intervention in patients requiring oral anticoagulation

Compared with OAC therapy alone, the addition of DAPT to OAC therapy results in a two- to three-fold increase in bleeding complications, suggesting that every effort should be undertaken to avoid bleeding (*Table 8*).[753] Assessing the balance of ischaemic and bleeding risks of relatively short (i.e. ≤6 months) triple therapy duration compared with double therapy consisting of clopidogrel and an OAC

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requires patient-by-patient decisions. Of note, previous randomized studies evaluating the duration of triple therapy or the benefit of NOACs vs. vitamin K antagonists (VKAs) were not adequately powered to assess ischaemic events, and data are lacking on the efficacy of dual therapy in patients at high risk of stroke or recurrent ACS.[754–757] In the major trials, there was no interaction between the duration of triple therapy and clinical presentation (ACS vs. no ACS). The rate of bleeding events peaked within the first 30 days of initiation of triple therapy, and was twice as high when compared with the rate of acute coronary events including recurrent MI and stent thrombosis. For these reasons, the duration of triple therapy should be minimized depending on bleeding and ischaemic risks (see *Tables 8 to 10* for guidance in decision-making). In stabilized event-free patients, discontinuation of any antiplatelet agent at 1 year after stenting is encouraged, while dual therapy may be continued beyond 1 year according to the stent-driven risk shown in *Table 9*.

Based on the favourable bleeding risk in the large phase 3 studies, a NOAC should be preferred over a VKA. The PIONEER[756] (Prevention of bleeding in patients with AF undergoing PCI) trial and the more recent RE-DUAL (Randomised Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patients with Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention)[757] trial compared a NOAC plus single antiplatelet therapy with triple therapy with a VKA plus DAPT and consistently showed significantly lower bleeding risks with the dual antithrombotic regimen. In RE-DUAL, both dosing regimens for dabigatran (150 mg and 110 mg b.i.d.) vs. warfarin triple therapy were associated with a significant reduction of major or clinically relevant bleeding events. However, as compared with triple therapy, an increase in both MI (4.5 vs. 3.0%, $P = 0.09$) and stent thrombosis risk (1.5 vs. 0.8%, $P = 0.15$) was reported for the lower dabigatran dose (110 mg b.i.d.), but not for the higher dabigatran dose (150 mg b.i.d.). Although statistical significance was missed, these findings raise concern about the efficacy of the lower dabigatran dose in combination with single antiplatelet therapy in preventing coronary events. Thus, the 150 mg b.i.d. dose of dabigatran is preferred. At present, evidence for a dual treatment approach is available for VKA,[755] rivaroxaban,[756] and dabigatran,[757] but none of these studies were powered to assess the efficacy of preventing stent thrombosis or thrombo-embolic events and only RE-DUAL used a NOAC dose that was previously shown to be effective in the prevention of thrombo-embolic events. The ongoing AUGUSTUS trial (ClinicalTrials.gov Identifier: NCT02415400) will address the value of apixaban in a similar setting, and with and without aspirin. Edoxaban is currently being investigated in a setting of triple treatment in the ENTRUST-AF-PCI (Evaluation of the safety and efficacy of an edoxaban-based antithrombotic regimen in patients with atrial fibrillation following successful percutaneous coronary intervention) trial (ClinicalTrials.gov Identifier: NCT02866175).

Figure 11 illustrates applicable DAPT algorithms in patients with an indication for OAC undergoing PCI with the respective classes of recommendations for the different treatment regimens. For more details on the pertinent studies in the field of triple treatment (DAPT plus OAC) and the associated issues, we refer the reader to the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[410]

Table 8 Strategies to avoid bleeding complications in oral anticoagulation patients

Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, and HAS-BLED) with a focus on modifiable risk factors.
Keep triple therapy duration as short as possible; dual therapy after PCI (OAC and clopidogrel) to be considered instead of triple therapy.
One should consider the use of a NOAC instead of a VKA when NOACs are not contraindicated.
Consider a target INR in the lower part of the recommended target range and maximize time in the therapeutic range (i.e. >65%) when a VKA is used.
Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
Use low-dose (≤100 mg daily) aspirin.
Routine use of PPIs.

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Adapted from Valgimigli et al.[410]
ABC = Age, Biomarkers, Clinical history; CHA2DS2-VASc = Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, prior Stroke or transient ischaemic attack or thromboembolism (doubled), Vascular disease, Age 65–74 years, Sex category (female); HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; INR = international normalized ratio; NOAC = non-vitamin K antagonist OAC; OAC = oral anticoagulant; PPIs = proton pump inhibitors; VKA = vitamin K antagonist.

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Table 9 High-risk features for ischaemic events

Prior stent thrombosis on adequate antiplatelet therapy
Stenting of the last remaining patent coronary artery
Diffuse multivessel disease, especially in diabetic patients
Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
At least three stents implanted
At least three lesions treated
Bifurcation with two stents implanted
Total stented length >60 mm
Treatment of a chronic total occlusion
History of STEMI

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STEMI = ST-elevation myocardial infarction.

Table 10 Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

Short life expectancy
Ongoing malignancy
Poor expected adherence
Poor mental status
End-stage renal failure
Advanced age
Prior major bleeding/prior haemorrhagic stroke
Chronic alcohol abuse
Anaemia
Clinically significant bleeding on dual antithrombotic therapy

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Dual antiplatelet therapy duration in patients with indication for oral anticoagulation

Recommendations	Class[a]	Level[b]
It is recommended that periprocedural aspirin and clopidogrel are administered to patients undergoing coronary stent implantation.	I	C
In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel, and an OAC should be considered for 1 month, irrespective of the type of stent used.[755]	IIa	B
Triple therapy with aspirin, clopidogrel, and an OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.[755]	IIa	B
Dual therapy with clopidogrel 75 mg/day and an OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.[754,756,757]	IIa	A
In patients with non-valvular AF requiring anticoagulation and antiplatelet treatment, a NOAC should be preferred over VKAs.[758–760]	IIa	A
In patients with an indication for a VKA in combination with aspirin and/or clopidogrel, the dose intensity of the VKA should be carefully regulated with a target INR in the lower part of the recommended target range and time in the therapeutic range >65%.[754,755]	IIa	B
Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.[753]	IIa	B
When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AF trials should be considered.[c]	IIa	C
When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg q.d. may be used instead of rivaroxaban 20 mg q.d.[756]	IIb	B
When dabigatran is used in combination with aspirin or clopidogrel, a dose of 150 mg b.i.d. may be preferred over a dose of 110 mg b.i.d.[757]	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and an OAC.	III	C

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ACS = acute coronary syndrome; AF = atrial fibrillation; b.i.d. = twice daily; INR = international normalized ratio; OAC = oral anticoagulant; NOAC = non-vitamin K oral anticoagulant; q.d. = once daily; VKA = vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

[c]Apixaban 5 mg b.i.d. or apixaban 2.5 mg b.i.d. if at least two of the following: age ≥80 years, body weight ≤60 kg, or serum creatinine level ≥1.5 mg/dL (133 µmol/L); dabigatran 110 mg or 150 mg b.i.d.; and edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: creatinine clearance of 30–50 mL/min; body weight ≤60 kg; concomitant use of verapamil, quinidine, or dronedarone; and rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if creatinine clearance 30–49 mL/min.

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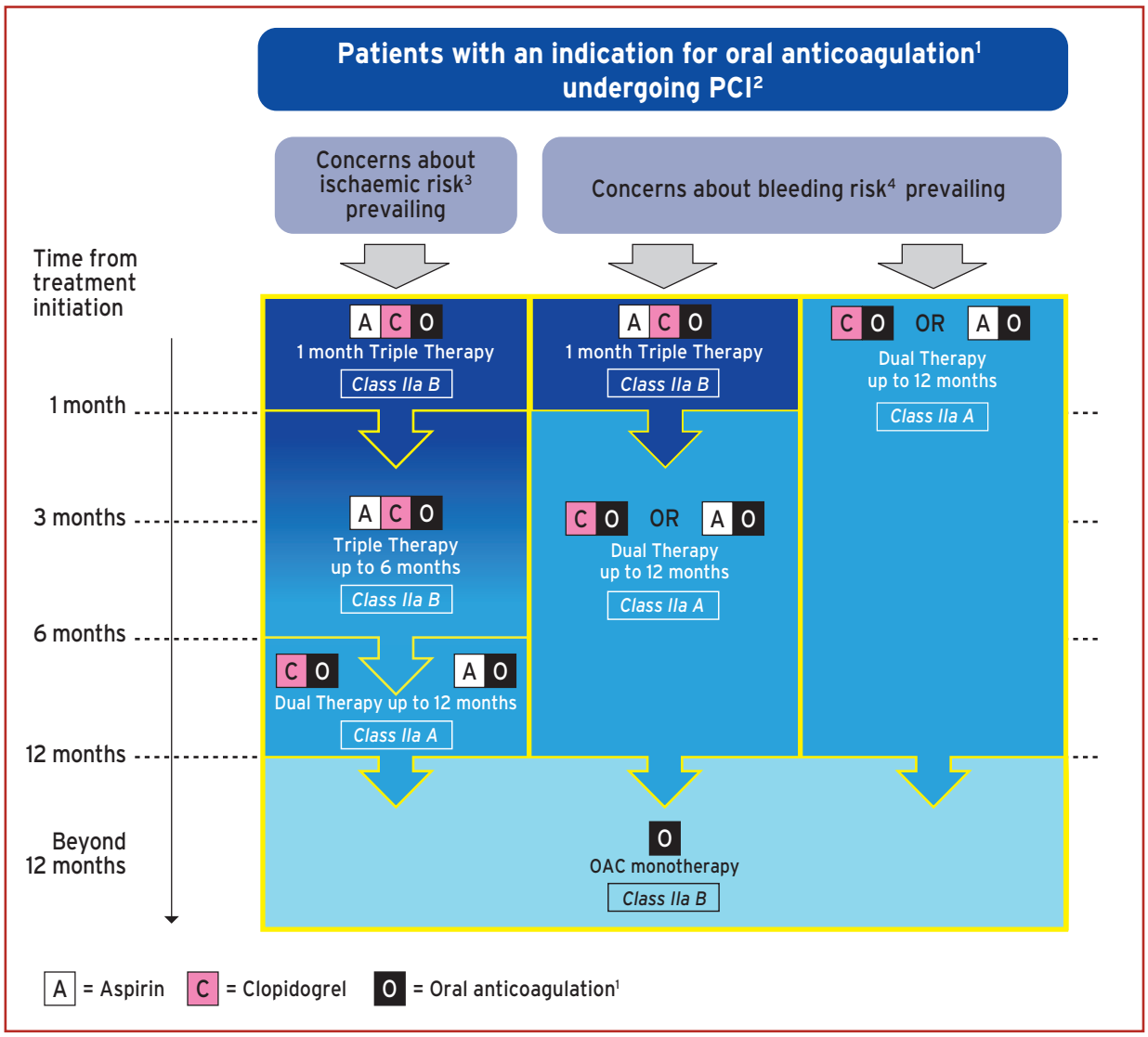

Colour-coding refers to the number of concomitant antithrombotic medication(s). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment with a single antiplatelet agent (aspirin or clopidogrel) plus OAC.
ABC = Age, Biomarkers, Clinical history; AF = atrial fibrillation; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; VKA = vitamin K antagonist.
[1]Non-vitamin K antagonist oral anticoagulant (NOAC) preferred over VKA in patients with non-valvular AF. (Class IIaA).
[2]Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy.
[3]High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.
[4]Bleeding risk can be estimated by HAS-BLED or ABC score.

Figure 11 Algorithm for dual antiplatelet therapy in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention.

17.5.2 Revascularization in patients with renal failure

See the Supplementary Data.

17.5.3 Monitoring of antiplatelet drugs (platelet function testing and genotyping)

See the Supplementary Data.

17.5.4 Surgery in patients on dual antiplatelet therapy

See 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[410]

17.6 Gaps in the evidence

The value of pre-hospital pre-treatment with prasugrel in STEMI patients, as well as the safety and efficacy of ticagrelor given at

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hospital admission in NSTE-ACS patients, has not been addressed in dedicated randomized studies.

The safety and efficacy of short-term potent antiplatelet treatment with either prasugrel or ticagrelor in SCAD patients is unknown, and is subject to ongoing clinical trials [the ALPHEUS (Assessment of Loading With the $P2Y_{12}$ Inhibitor Ticagrelor or Clopidogrel to Halt Ischemic Events in Patients Undergoing Elective Coronary Stenting) trial: NCT02617290 and the SASSICAIA (Comparison of Loading Strategies With Antiplatelet Drugs in Patients Undergoing Elective Coronary Intervention) trial: NCT02548611].

The clinical benefit of a short-term DAPT duration followed by long-term ticagrelor monotherapy (and stopping aspirin) remains unknown. The ongoing GLOBAL LEADERS (Long-term ticagrelor monotherapy versus standard dual antiplatelet therapy followed by aspirin monotherapy in patients undergoing biolimus-eluting stent implantation) and TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention) trials aim to close this gap in our current knowledge (NCT01813435 and NCT02270242, respectively).

18 Volume outcome relationship for revascularization procedures

Operator experience influences outcomes, particularly in critical, complex situations. Greater total experience of an entire hospital team—consisting of the supporting members in the operating room or catheterization laboratory and those responsible for postoperative care—results in more favourable outcomes.

18.1 Coronary artery bypass grafting

Studies have suggested that the volume of CABG surgery in a hospital significantly impacts in-hospital mortality, although no consistent cut-offs for volume were used in these studies.[761–762] This increase in mortality observed in lower volume centres seems to be attributable to so-called 'failure to rescue': although patients operated on at low-volume centres are not at particularly higher risk of suffering a major complication, they are more likely to die from such a complication should it occur.[763] Therefore, consideration should be given to the performance of CABG in centres with an annual volume of at least 200 CABG cases. Apart from hospital volume, higher surgeon volume also appears to be inversely related to operative mortality. Birkmeyer *et al*. provided evidence suggesting that both hospitals and surgeons have some impact on outcomes.[764]

Several studies suggest that quality measures are more important than volume *per se*.[765,766] Missing quality indicators in hospitals strongly predicted mortality, irrespective of surgeon or hospital case volumes.[767] Therefore, it is recommended that such quality measures (as an example see Supplementary *Table 9*) are adopted and reported to facilitate focused quality improvement.[768]

18.2 Percutaneous coronary intervention

Numerous studies have investigated the relationship between the volume of procedures and outcomes of PCI, suggesting a volume–outcome relationship at the operator level, as well as at the institutional level.[761,769–773] A population-based study from the PCI reporting system of New York indicated that hospital case volumes <400 PCIs per year and operator case volumes <75 PCIs per year were associated with impaired outcomes.[769]

Among patients with ACS, particularly STEMI, operator and hospital volumes play important roles. A large study in the USA reported that, in a cohort of 36 535 patients undergoing primary PCI, in-hospital mortality was significantly lower in institutions with higher primary PCI volumes (5.7% in hospitals performing >33 primary PCIs/year vs. 7.7% in hospitals performing <12 primary PCIs/year).[774]

Operator volume has also been shown to impact outcomes in LM PCI. A single-centre study of 1948 patients who underwent unprotected LM PCI, performed by 25 operators over a 7 year period, showed reduced 30 day and 3 year mortality for patients who had their PCI performed by a high-volume operator (defined as ≥15 LM PCI/year; mean 25/year) vs. a low-volume operator (<15 LM PCI/year).[775]

An example of quality measures for PCI is provided in Supplementary *Table 10*.

18.3 Training in cardiac surgery and interventional cardiology for myocardial revascularization

A European training programme in interventional cardiology has been proposed by the EAPCI in order to ensure the high quality of patient care and clinical excellence.[776] The programme should last 1–2 years at high-volume institutions that handle ≥800 PCIs per year and that have an established 24 h/7 day service for the treatment of patients with ACS.

For CABG, no standardized European programme exists at this time. However, the pace at which proficiency reaches certain acceptable standards differs from trainee to trainee. Therefore, although it is recommended that trainees perform ≥200 CABG procedures under supervision before becoming completely independent, a competency-driven residency programme with regular evaluation of progress is recommended over a volume-driven programme.

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Recommendations for operator/institutional volume in myocardial revascularization

Recommendations	Class[a]	Level[b]
CABG		
It should be considered that CABG be performed at institutions with annual institutional volumes of ≥200 CABG cases.	IIa	C
PCI		
It should be considered that PCI for ACS be performed by trained operators with annual volumes of ≥75 procedures at institutions performing ≥400 PCIs per year with an established 24 h/7 day service for the treatment of patients with ACS.	IIa	C
It should be considered that PCI for SCAD be performed by trained operators with annual volumes of ≥75 procedures at institutions performing ≥200 PCIs per year.	IIa	C
It should be considered that institutions with annual volumes of <400 PCIs collaborate in networks with higher-volume institutions (>400 PCIs per year), with shared written protocols and exchange of operators and support staff.	IIa	C
It should be considered that PCI for LM be performed by trained operators with an annual volume of ≥25 LM PCI cases per year.	IIa	C
It should be considered that non-emergency high-risk PCI procedures—such as for LM disease, single remaining patent coronary artery, and complex chronic total occlusions—are only performed by adequately experienced operators at centres that have access to circulatory support and intensive care treatment.	IIa	C

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ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; LM = left main; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations for training in myocardial revascularization

Recommendations	Class[a]	Level[b]
Training in CABG		
It is recommended that trainees in cardiac surgery and interventional cardiology follow a competency-driven residency programme with regular evaluation of progression.	I	C
It should be considered that trainees in cardiac surgery perform ≥200 CABG procedures under supervision before being independent.	IIa	C
Training in PCI		
It should be considered that trainees in interventional cardiology perform ≥200 PCI procedures as first operator, with one-third of PCI procedures in emergency or ACS patients under supervision, before being independent.	IIa	C
It should be considered that trainees in interventional cardiology complete formal training according to a 1–2 year curriculum at institutions with ≥800 PCIs per year and an established 24 h/7 day service for the treatment of patients with ACS.	IIa	C

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ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.

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Recommendations for outcome registration, monitoring, and benchmarking

Recommendations	Class[a]	Level[b]
It is recommended that specific quality performance measures for CABG are adopted at a national level to allow outcome monitoring and benchmarking.	I	C
It is recommended that national societies establish national databases on CABG practice and outcomes.	I	C
It is recommended that CABG outcome data are reported by hospitals to national databases.	I	C

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CABG = coronary artery bypass grafting.
[a]Class of recommendation.
[b]Level of evidence.

19 Medical therapy, secondary prevention, and strategies for follow-up

Myocardial revascularization must be accompanied by medical therapy and other secondary prevention strategies for risk factor modification and permanent lifestyle changes.[42] Secondary prevention and cardiac rehabilitation are an integral part of management after revascularization because such measures reduce future morbidity and mortality in a cost-effective way, and can further improve symptoms. These measures are discussed in detail in the European Guidelines on Cardiovascular Disease Prevention that were published in 2016.[42]

The need to detect restenosis has reduced in the DES era. Likewise, the durability of CABG results have increased with the use of arterial grafts, and ischaemia stems mainly from SVG attrition and/or progression of CAD in native vessels. Nevertheless, the recurrence of symptoms or ischaemia due to disease progression or restenosis deserves attention.

Strategies for follow-up and management in patients after myocardial revascularization

Recommendations	Class[a]	Level[b]
After CABG or PCI for AMI, participation in a cardiac rehabilitation programme is recommended to improve patient outcomes.[777]	I	A
It is recommended that secondary prevention measures, including medical therapy and lifestyle changes, are started and reinforced after myocardial revascularization.[683,778–785]	I	A
It is recommended that patients are re-evaluated after myocardial revascularization (e.g. at 3 months and thereafter, at least on an annual basis) in order to reassess symptoms and adherence to secondary prevention measures, and reinforce medical therapy and lifestyle changes when appropriate.	I	C
Symptomatic patients		
Coronary angiography is recommended in patients with intermediate- to high-risk findings[c] at stress testing.	I	C
An imaging stress test should be considered in patients with prior revascularization over stress ECG.[786]	IIa	B
Asymptomatic patients		
Surveillance by non-invasive imaging-based stress testing may be considered in high-risk patient subsets 6 months after revascularization.	IIb	C
After high-risk PCI (e.g. unprotected LM stenosis), late (3–12 months) surveillance angiography may be considered, irrespective of symptoms.	IIb	C
Routine non-invasive imaging-based stress testing may be considered 1 year after PCI and >5 years after CABG.	IIb	C

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AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; ECG = electrocardiogram; LM = left main; PCI = percutaneous coronary intervention.
[a]Class of recommendation.
[b]Level of evidence.
[c]Intermediate- and high-risk findings at stress imaging are ischaemia at low workload with exercise stress testing, early-onset ischaemia with pharmacological stress testing, an inducible wall motion abnormality, or a reversible perfusion defect in ≥10% of LV myocardium.

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19.1 Gaps in the evidence

In all studies to date on the optimal follow-up after PCI, the gain from discovering patients with restenosis is obscured by the high rate of false positive exercise ECG tests indicating ischaemia. Therefore, simple exercise ECG testing is not recommended for follow-up and a non-invasive imaging approach is preferred. Specific studies to clarify which subset of patients benefits more from a specific follow-up approach are missing. More studies are needed to assess the role of CT angiography in patient surveillance after myocardial revascularization.

20 Key messages

(1) Myocardial revascularization is performed for the relief of symptoms of myocardial ischaemia and the improvement of prognosis. In SCAD, the prognostic benefit is dependent on the extent of myocardium subject to ischaemia.

(2) The prognostic and symptomatic benefits of myocardial revascularization critically depend on the completeness of revascularization. Therefore, the ability to achieve complete revascularization is a key issue when choosing the appropriate treatment strategy.

(3) Apart from issues of individual operative risk and technical feasibility, diabetes mellitus and the anatomical complexity of CAD determine the relative benefits of PCI and CABG.

(4) The SYNTAX score is the recommended tool to gauge the anatomical complexity of coronary disease.

(5) In some instances, both PCI and CABG are equally reasonable, or sometimes even equally problematic, options. This calls for the Heart Team to be consulted to develop individualized treatment concepts, with respect for the preferences of the patient who has been informed about early and late outcomes.

(6) Timely PCI of the culprit lesion remains the mainstay of treatment of ACS.

(7) After PCI of the culprit lesion in ACS, the choice of further revascularization modality should follow the criteria applied to patients with SCAD.

(8) Radial access is preferred for any PCI irrespective of clinical presentation, unless there are overriding procedural considerations.

(9) DES are recommended for any PCI irrespective of clinical presentation, lesion type, anticipated duration of DAPT, or concomitant anticoagulant therapy.

(10) Even though 6 months of DAPT is generally recommended after PCI in SCAD and 12 months of DAPT after ACS, the type and duration of DAPT should be individualized according to the ischaemic and bleeding risks, and appropriately adapted during follow-up. Based on this judgement, treatment durations for DAPT after DES that are as short as 1 month or even as long as lifelong may be reasonable.

(11) Off-pump surgery with no-touch aorta for high-risk patients should be considered when expertise exists.

(12) Multiple arterial grafting should be considered using the radial artery for high-grade stenosis and/or BIMA grafting for patients who do not have an increased risk of sternal wound infection.

21 Evidence-based 'to do' and 'not to do' messages from the Guidelines

Risk models to assess short- and long-term outcomes after myocardial revascularization		Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.		I	A
It is recommended that the STS score is calculated to assess in-hospital or 30 day mortality, and in-hospital morbidity, after CABG.		I	B
In patients with LM or multivessel disease, it is recommended that the SYNTAX score is calculated to assess the anatomical complexity of CAD and the long-term risk of mortality and morbidity after PCI.		I	B
Indications for revascularization in patients with stable angina or silent ischaemia			
For prognosis	LM disease with stenosis >50%.[c]	I	A
	Any proximal LAD stenosis >50%.[c]	I	A
	Two- or three-vessel disease with stenosis >50%[c] with impaired LV function (LVEF ≤35%).[c]	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR.[d]	I	B
For symptoms	Any haemodynamically significant coronary stenosis in the presence of limiting angina or angina equivalent, with an insufficient response to optimized medical therapy.	I	A

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Type of revascularization (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality				
Recommendations according to the extent of CAD	**CABG**		**PCI**	
	Class[a]	**Level[b]**	**Class[a]**	**Level[b]**
One-vessel CAD				
With proximal LAD stenosis	I	A	I	A
Two-vessel CAD				
With proximal LAD stenosis	I	B		
LM CAD				
LM with low SYNTAX score 0 - 22	I	A	I	A
LM with intermediate SYNTAX score >22 and ≤32	I	A		
LM with high SYNTAX score >32.[e]	I	A	III	B
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score 0 - 22	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score >22[e]	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0 - 22	I	A		
Three-vessel disease with intermediate or high SYNTAX score >22[e]	I	A	III	A
Invasive evaluation and revascularization in NSTE-ACS				
An early invasive strategy (<24 h) is recommended in patients with at least one high-risk criterion (*Figure 4*).			I	A
An invasive strategy (<72 h after first presentation) is indicated in patients with at least one intermediate-risk criterion (*Figure 4*) or recurrent symptoms.			I	A
It is recommended that the revascularization strategy (*ad hoc* culprit-lesion PCI/multivessel PCI/CABG) is based on the patient's clinical status and comorbidities, as well as the disease severity, i.e. distribution and angiographic lesion characteristics (e.g. SYNTAX score), according to the principles for SCAD.			I	B
In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended during primary PCI.			III	B

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Primary PCI for myocardial reperfusion in STEMI		
Indication		
Reperfusion therapy is indicated in all patients with time from symptom onset <12 h duration and persistent ST-segment elevation.	I	A
A primary PCI strategy is recommended over fibrinolysis within indicated timeframes.	I	A
Logistics		
It is recommended that the pre-hospital management of STEMI patients be based on regional networks that are designed to timely and effectively deliver reperfusion therapy, and to offer primary PCI to as many patients as possible.	I	B
It is recommended that primary PCI-capable centres deliver a 24 h/7 day service and ensure that primary PCI is performed as fast as possible.	I	B
Patients transferred to a PCI-capable centre for primary PCI should bypass the emergency department and be transferred directly to the catheterization laboratory.	I	B
Strategy/technique		
In cardiogenic shock, routine revascularization of non-IRA lesions is not recommended during primary PCI.	III	B
Routine use of thrombus aspiration is not recommended.	III	A
Recommendations on revascularizations in patients with chronic heart failure and systolic LV dysfunction (EF ≤35%)		
In patients with severe LV systolic dysfunction and coronary artery disease suitable for intervention, myocardial revascularization is recommended.	I	B
CABG is recommended as the first revascularization strategy choice in patients with multivessel disease and acceptable surgical risk.	I	B
Revascularizations in patients with cardiogenic shock		
Emergency invasive evaluation is indicated in patients with acute heart failure or cardiogenic shock complicating ACS.	I	B
Emergency PCI is indicated for patients with cardiogenic shock due to STEMI or NSTE-ACS, independent of time delay of symptom onset, if coronary anatomy is amenable.	I	B
Emergency CABG is recommended for patients with cardiogenic shock if the coronary anatomy is not amenable to PCI.	I	B
Routine use of IABP in patients with cardiogenic shock due to ACS is not recommended.	III	B
Prevention of contrast-induced nephropathy		
Patients with moderate-to-severe CKD		
Use of low- or iso-osmolar contrast media is recommended.	I	A
It is recommended that the volume of contrast media is minimized.	I	B
Severe CKD		
Haemodialysis therapy is not recommended as a preventative measure.	III	B
Pre-operative strategies to reduce the incidence of stroke in patients undergoing CABG		
In patients undergoing CABG, carotid DUS is recommended in patients with recent (<6 months) history of stroke/TIA.	I	B

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Disease progression and late graft failure		
Repeat revascularization is indicated in patients with extensive ischaemia or severe symptoms despite medical therapy.	I	B
IMA is the conduit of choice for redo CABG in patients in whom the IMA was not used previously.	I	B
DES are recommended for the treatment of in-stent restenosis within BMS or DES.	I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis within BMS or DES.	I	A
Prevention of ventricular arrhythmias by revascularization		
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG consistent with STEMI.	I	B
Perioperative oral β-blocker therapy is recommended for the prevention of post-operative AF after CABG surgery.	I	B
Procedural aspects of CABG		
Arterial grafting with an IMA to the LAD system is recommended.	I	B
Use of the radial artery is recommended over the saphenous vein in patients with high-degree stenosis.	I	A
Skeletonized IMA dissection is recommended in patients with high risk of sternal wound infection.	I	B
Minimization of aortic manipulation is recommended.	I	B
Procedural aspects of PCI		
DES[f] are recommended over BMS for any PCI irrespective of: • clinical presentation • lesion type • planned non-cardiac surgery • anticipated duration of DAPT • concomitant anticoagulant therapy.	I	A
Radial access is recommended as the standard approach, unless there are overriding procedural considerations.	I	A
Stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch, is recommended for PCI of bifurcation lesions.	I	A
Antithrombotic treatment in SCAD patients undergoing PCI		
Treatment with 600 mg clopidogrel is recommended in elective PCI patients once anatomy is known and the decision has been made to proceed with PCI.	I	A
Aspirin is indicated before elective stenting.	I	A
Clopidogrel (600 mg loading dose and 75 mg daily maintenance dose) is recommended for elective stenting.	I	A
UFH is indicated as a standard anticoagulant (70–100 U/kg).	I	B
Life-long single antiplatelet therapy, usually aspirin, is recommended.	I	A
In patients with SCAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type.	I	A
Antithrombotic treatment in NSTE-ACS patients undergoing PCI		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.) and at a maintenance dose of 75–100 mg daily long-term, regardless of treatment strategy.	I	A

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A $P2Y_{12}$ inhibitor is recommended in addition to aspirin, maintained over 12 months unless there are contraindications such as an excessive risk of bleeding. Options are:	I	A
• Prasugrel in $P2Y_{12}$-naïve patients who proceed to PCI (60 mg loading dose and 10 mg daily dose)	I	B
• Ticagrelor irrespective of the pre-treatment and revascularization strategy (180 mg loading dose, 90 mg twice daily)	I	B
• Clopidogrel (600 mg loading dose and 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B
Pre-treatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended.	III	A
Administration of prasugrel to patients in whom coronary anatomy is not known is not recommended.	III	B
Peri-interventional anticoagulation is recommended for all patients in addition to antiplatelet therapy.	I	A
In patients on fondaparinux (2.5 mg daily s.c.), a single bolus UFH (85 IU/kg, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) is indicated.	I	B
Crossover of UFH and LMWH is not recommended.	III	B
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as an excessive risk of bleeding (e.g. PRECISE-DAPT ≥25).	I	A
Antithrombotic treatment in STEMI patients undergoing PCI		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contraindicated, is recommended before (or at the time of PCI at the latest) PCI and should be maintained over 12 months, unless there are contraindications such as an excessive risk of bleeding.	I	A
Strategies for follow-up and management		
After CABG or PCI for AMI, participation in a cardiac rehabilitation programme is recommended to improve patient outcomes.	I	A
It is recommended that secondary prevention measures, including medical therapy and lifestyle changes, are started and reinforced after myocardial revascularization.	I	A

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ACS = acute coronary syndrome; AF = atrial fibrillation; AMI = acute myocardial infarction; BMS = bare-metal stent; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CKD = chronic kidney disease; DAPT = dual antiplatelet therapy; DES = drug eluting stents; DUS = duplex ultrasound; ECG = electrocardiogram; EF = ejection fraction; FFR = fractional flow reserve; GP = glycoprotein; IABP = intra-aortic balloon pump; iwFR = instantaneous wave-free radio; IMA = internal mammary artery; IRA = infarct-related artery; i.v. = intravenous; LAD = left anterior descending; LM = left main; LMWH = low-molecular-weight heparin; LV = left ventricular; LVEF = left ventricular ejection fraction; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; s.c. = subcutaneous; SCAD = stable coronary artery disease; STEMI = ST-elevation myocardial infarction; STS = Society of Thoracic Surgeons; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; TIA = transient ischaemic attack; UFH = unfractionated heparin.

[a]Class of recommendation.

[b]Level of evidence.

[c]With documented ischaemia, a haemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89, or >90% stenosis in a major coronary vessel.

[d]Based on FFR <0.75 indicating a prognostically relevant lesion.

[e]PCI should be considered, if the Heart Team is concerned about the surgical risk or if the patient refuses CABG after adequate counselling by the Heart Team.

[f]These recommendations refer to stents that are supported by large-scale randomized trials with clinical endpoint evaluation leading to an unconditional CE mark.

22 Appendix

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