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ESC/EACTS GUIDELINES

# 2014 ESC/EACTS Guidelines on myocardial revascularization

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

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

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#### 16.3.6 On-pump and off-pump procedures

Despite improved techniques and experience, part of the morbidity related to CABG is caused by the extracorporeal circulation (cardiopulmonary bypass) and access for cardiopulmonary bypass, prompting the off-pump approach. Two recent 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.[441,621,622] There is also enough evidence to conclude that, for most patients and surgeons, on-pump CABG provides the best—or equal—short- and long-term outcomes.[621–625] For some surgeons, off-pump CABG is associated with inferior early and late graft patency rates and possibly compromised long-term survival; however, complete off-pump procedures in the hands of highly trained teams appear to be associated with a reduced risk of early morbidity, such as stroke, wound and respiratory infections, as well as fewer transfusions and shorter hospital stay.[626–629] In the subgroup of patients with end-stage CKD, there is some evidence that off-pump CABG is associated with lower in-hospital mortality and need for new renal replacement therapy.[380]

In the subgroup of patients with atherosclerotic changes of the ascending aorta, a no-touch technique—avoiding any manipulations of the ascending aorta either on- or off-pump—is essential to reduce the risk of stroke.[443] The consistent cross-over rate of around 5% from on-pump CABG to off-pump CABG in high-quality RCTs suggests the necessity of routine ECG-gated CT scans of the thoracic aorta before bypass surgery in patients over 70 years of age or those with other risk factors for extensive atherosclerosis.

#### 16.3.7 Minimally invasive procedures

Minimally invasive direct coronary artery bypass may represent an attractive alternative to a sternotomy.[630] It has a similar safety and efficacy profile to conventional on- and off-pump CABG, with 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.[631–633]

### 16.4 Reporting perioperative outcome

Perioperative reporting of outcome after CABG procedures should be done on a risk-adjusted basis. Early clinical outcome at 3 months after CABG is characterized by a 1–2% mortality rate and a 1–2% morbidity rate for each of the following events: stroke, renal, pulmonary and cardiac failure, bleeding, and wound infections. The early risk period after CABG extends up to 3 months, is multifactorial, and depends on the interface between technical variability and patient comorbidity.[634]

## 17. Procedural aspects of percutaneous coronary intervention

### 17.1 Percutaneous coronary intervention devices

#### 17.1.1 Balloon angioplasty

Plain balloon angioplasty has been displaced in the treatment of *de novo* coronary lesions after demonstration of the superiority of BMS and, more recently, DES in terms of repeat revascularization.[645] Its contribution to the treatment of in-stent restenosis has also diminished after recent studies demonstrated the advantages of DES and drug-coated balloons for this indication.[505,511] However, balloon angioplasty might be a valuable PCI option in all patients in whom implantation of stents is technically not achievable, or in a vessel that is too small to be stented (<2.0 mm), and in patients with critical stenoses who require urgent surgery.

#### 17.1.2 Coronary stents

**Bare-metal stents**

Coronary stents are very effective in repairing dissections and have eliminated the need for urgent CABG due to abrupt vessel closure. Fully covered stents can be life-saving in the rare event of coronary perforation. The contribution of BMS is its approximately 30% lower rate of restenosis than with plain balloon angioplasty.[645] Although many efforts have been made to further reduce restenosis by modification of stent design and materials, thinning of stent struts has been the only proven modification capable of reducing restenosis of BMS.[646,647] Bare-metal stents have been associated with favourable outcomes in terms of mortality, myocardial infarction, and stent thrombosis.[124] However, owing to a 20–30% rate of recurrence of angiographic stenosis within 6–9 months after implantation, restenosis with BMS has often been referred to as the 'Achilles' heel' of PCI.[645] There is no indication for BMS over new-generation DES, irrespective of patient and lesion subset. Similarly, there is no clear evidence of a difference between DES and BMS in the risk of stent thrombosis following unplanned disruption of DAPT.[648]

**Early-generation drug-eluting stents**

The risk of restenosis with BMS led to the development of DES, which consist of a metallic stent platform with controlled release of antiproliferative drugs, mostly controlled by surface polymers. Early-generation DES released sirolimus (e.g. Cypher®)[649] or paclitaxel (e.g. Taxus®).[650] Both in native vessels and saphenous vein bypass grafts, DES potently reduced angiographic and ischaemia-driven TVR.[124,495] Thus, the risk of clinical restenosis with the use of early-generation DES was 50–70% lower than with BMS, corresponding to a number-needed-to-treat of approximately 7–8.[124] In RCTs, no significant differences were observed in the long-term rates of death or myocardial infarction after use of DES or BMS.[124,199] Despite the superior anti-restenotic efficacy of early-generation DES over BMS, concerns have been generated by studies showing an increased propensity for very late stent thrombosis.[244,651,652] Although early-generation DES represented an important advance in the field of PCI,[653] they currently play an irrelevant role in the treatment of CAD and are largely supplanted by new-generation DES.[3]

**New-generation drug-eluting stents**

New-generation DES are characterized by thin-strut, metallic platforms that release limus-based antiproliferative drugs from durable polymers with improved biocompatibility and lower polymer mass,[654,655] biodegradable polymers,[654,656–658] or polymer-free surfaces.[659,660] Recent studies have shown the superiority of several new-generation DES over early-generation DES, not only with respect to efficacy but also safety.[128,129,661,662] New-generation DES have addressed previous concerns of very late

stent thrombosis and are at least as safe as bare-metal stents during long-term follow-up. *Table 10* displays a list of Conformité Européenne (CE)-approved new-generation DES, supported by RCT evidence with clinical endpoints. *Table 11* shows a list of CE-approved new-generation DES, the proven efficacy of which was based on angiographic findings from studies with or without a control group. These tables only provide a temporary 'snapshot' of available products, as new devices will be introduced or new evidence of established devices will become available.

**Indications for new-generation DES**

Increased efficacy and safety of new-generation DES have enabled their unrestricted use in patients with CAD and an indication for PCI, including patients with diabetes, multivessel and LM disease, acute myocardial infarction, SVG and restenotic lesions, and chronic total occlusions.[3] New-generation DES should therefore be considered by default in all clinical conditions and lesion subsets. Among patients who require anticoagulation with NOACs, undergo non-cardiac surgery, experience bleeding complications, or are non-compliant with medication intake, previous concerns relating to differences in the duration of DAPT and risks associated with DAPT cessation are not substantiated in recent data sets.[648,663]

### 17.1.3 Bioresorbable stents

Completely bioresorbable stents, which dissolve after fulfilling their support function in the lesion site of the coronary vessel, have been a perennial aim since the introduction of the metallic stents. The combination of resorbable stent platforms with drug-eluting properties has enhanced the efficacy of these devices. Current stent platforms are based on two technologies: the manufacturing of drug-eluting, bioresorbable, polymer-based stents and drug-eluting, resorbable, metallic (magnesium) stents.[684] The resorption process of the stent platforms takes from several months to 2 years, depending on polymer composition. To date, bioresorbable stents have been shown to dissolve completely over time, to restore the vasomotion of treated segments, and to result in positive remodelling with late lumen enlargement. In small series of patients with relatively simple lesions, early results are promising and appear to be similar to new-generation DES.[685–687] However, confirmation in large-scale RCTs is required to establish the indications for these devices. *Table 12* includes the list of devices approved for use in Europe.

### 17.1.4 Drug-coated balloons

The rationale of using drug-coated balloons 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. Using a paclitaxel-coated balloon, three RCTs, Paclitaxel-Coated Balloon Catheter I (PACCOCATH-I) and PACCOCATH–II,[507,508] and Paclitaxel-Eluting PTCA–Catheter In Coronary Disease (PEPCAD)-II,[689] have targeted in-stent restenosis following BMS implantation, while three others have targeted in-stent restenosis in patients predominantly treated with DES eluting limus-analogues.[509–511] By virtue of the positive results achieved without additional stent implantation, drug-coated balloons may represent an attractive option for patients with restenosis after implantation of DES, although it is not known whether they are as safe and effective for this indication as new-generation DES that elute limus analogues.

In the randomized PEPCAD III study, the combination of a drug-coated balloon with cobalt chromium stent implantation was inferior to a sirolimus-eluting stent for *de novo* indications.[690] Also, the Drug Eluting Balloon in Acute Myocardial Infarction (DEB-AMI) trial showed that drug-coated balloons followed by BMS implantation were inferior to paclitaxel-eluting stents in patients with STEMI.[691] A recent angiographic study suggested that drug-coated balloons may serve as an alternative to paclitaxel-eluting stents for the treatment of lesions in small coronary vessels;[692] however, the role of drug-coated balloons in this setting has not been evaluated against more effective, new-generation DES with limus analogues. There are various types of drug-coated balloons approved for use in Europe and their main characteristics are listed in *Table 13*. Most of the differences are related to the drug carrier, whereas paclitaxel is currently the sole active drug used. Although specifically designed comparative studies are lacking, one cannot assume a class effect for all drug-coated balloons.[693]

### 17.1.5 Other devices

Although routine use of rotational atherectomy did not improve outcomes after DES,[698] such a device might technically be required in cases of tight and calcified lesions, to allow subsequent passage of balloons and stents. There is a resurgence in the use of rotational atherectomy for the purpose of optimal lesion preparation among patients undergoing implantation of bioresorbable stents.

## 17.2 Adjunctive invasive diagnostic tools

### 17.2.1 Intravascular ultrasound

Coronary angiography is unable to visualize the atherosclerotic involvement of the arterial wall. Intravascular ultrasound imaging allows a real-time, tomographic assessment of lumen area and plaque composition, size, and distribution. As a result of diffuse disease and remodelling, coronary angiography underestimates the extent and severity of the disease compared with IVUS.[699] Although invasive by nature, IVUS is the established standard for accurate measurement of plaque burden, and the technique has been systematically used to determine the influence of different drugs on coronary plaque progression or regression.[700,701]

Several RCTs addressed the potential of IVUS in reducing restenosis and adverse events after BMS implantation—with conflicting results. Most of these RCTs focussed on optimizing stent expansion using IVUS. Findings from meta-analyses subsequently suggested that better clinical and angiographic results may be obtained under IVUS guidance.[702–704] In the DES era, a threshold of stent expansion (5.0–5.5 $mm^2$) was proposed to predict the occurrence of late events. In the subset of patients with LM disease, observational studies suggest that IVUS-guided stent implantation is associated with improved survival during long-term clinical follow-up.[705] The use of intracoronary imaging has also been advocated in patients with stent failure, including restenosis and stent thrombosis, in order to explicate and correct underlying mechanical factors. In a multicentre all-comers study to establish the frequency, predictors, and timing

**Table 10 CE-approved new-generation DES recommended for clinical use based on randomized trials with a primary clinical endpoint (in alphabetical order)**

| DES | Stent platform | Polymer coating | Drug | References |
|---|---|---|---|---|
| **Based on durable polymer coatings** | | | | |
| Promus element | Platinum–chrome | PBMA and PVDF-HFP | Everolimus | 664,665 |
| Resolute | Cobalt–chrome | PBMA, PHMA, PVP, and PVA | Zotarolimus | 655,665,666 |
| Xience | Cobalt–chrome | PBMA and PVDF-HFP | Everolimus | 247, 654,667 |
| **Based on biodegradable polymer coatings** | | | | |
| Biomatrix | Stainless steel | PDLLA | Biolimus A9 | 248, 668 |
| Nobori | Stainless steel | PDLLA | Biolimus A9 | 656,658,669 |
| Yukon Choice PC | Stainless steel | PDLLA | Sirolimus | 657 |
| Orsiro | Cobalt-chrome | PLLA | Sirolimus | 961 |
| Ultimaster | Cobalt–chrome | PDLLA and PCL | Sirolimus | 960 |

CE = Conformité Européenne; DES = drug-eluting stent; PBMA = poly n-butyl methacrylate; PDLLA = poly(d,l)-lactic acid; PHMA = polyhexyl methacrylate; PLLA = poly-L-lactic acid; PVA = polyvinyl acetate; PVDF-HFP = poly(vinylidene fluoride-cohexafluoropropylene).

**Table 11 CE-approved DES with angiographic efficacy data from randomized or non-randomized studies (in alphabetical order)**

| DES | Stent platform | Polymer coating | Drug | References |
|---|---|---|---|---|
| **Based on durable polymer coatings** | | | | |
| DESyne Nx | Cobalt–chrome | PBMA | Novolimus | 670 |
| STENTYS | Nitinol | PSU and PVP | Paclitaxel | 671 |
| **Based on biodegradable polymer coatings** | | | | |
| Axxess | Nitinol | PDLLA | Biolimus A9 | 672,673 |
| BioMime | Cobalt–chrome | PLLA and PLGA | Sirolimus | 674 |
| Combo | Stainless steel | PDLLA and PLGA + Additional coating with anti-CD34 | Sirolimus | 675 |
| DESyne BD | Cobalt–chrome | PLLA | Novolimus | |
| Infinnium | Stainless steel | PLLA, PLGA, PCL, and PVP | Paclitaxel | 676 |
| MiStent | Cobalt–chrome | PLGA | Crystalline sirolimus | 677 |
| Supralimus Core | Cobalt–chrome | PLLA, PLGA, PCL, and PVP | Sirolimus | 678,679 |
| Synergy | Platinum-chrome | PLGA | Everolimus | 680 |
| **Polymer-free** | | | | |
| Amazonia Pax | Cobalt-chrome | – | Paclitaxel | |
| BioFreedom | Stainless steel | – | Biolimus A9 | |
| Cre8 | Cobalt–chrome | – | Sirolimus | 681 |
| Yukon Choice PF | Stainless steel | – | Sirolimus | 682,683 |

CE = Conformité Européenne; DES = drug-eluting stent; PBMA = poly n-butyl methacrylate; PCL = poly(L-lactide co-ϵ-caprolactone); PDLLA = poly(d,l)-lactic acid; PLGA = poly(lactide-co-glycolide); PLLA = poly-L-lactic acid; PSU = polysulfone; PVP = polyvinylpyrrolidone.

**Table 12 Bioresorbable stents providing drug-elution with angiographic efficacy data from non-randomized studies (in alphabetical order)**

| Device | Delivery platform | Polymer | Drug | References |
|---|---|---|---|---|
| Absorb BVS | PLLA | PDLLA | Everolimus | 685,686 |
| DESolve | PLLA | PLLA | Novolimus | 688 |
| DREAMS | Magnesium alloy | PLGA | Paclitaxel (revised version Sirolimus) | 687 |

PDLLA = poly(d,l)-lactic acid; PLGA = poly(lactide-co-glycolide); PLLA = poly-L-lactic acid.

**Table 13 CE-approved drug-coated balloons (in alphabetical order)**

| Device | Carrier | Drug | References |
|---|---|---|---|
| Danubio | BTHC | Paclitaxel | – |
| Dior II | Shellac | Paclitaxel | 694,695 |
| Elutax | – | Paclitaxel | 693 |
| IN.PACT Falcon | Urea | Paclitaxel | 692 |
| Moxy | Polysorbate | Paclitaxel | 696 |
| Pantera Lux | BTHC | Paclitaxel | 697 |
| Protégé NC | BTHC | Paclitaxel | – |
| SeQuent Please | Iopromide | Paclitaxel | 507–511 |

BTHC = butyryl-tri-hexyl citrate; CE = Conformité Européenne.

of stent thrombosis, a pre-specified substudy compared outcomes of IVUS against angiographic guidance of DES implantation.[706] IVUS-guided DES implantation (pre- and post-PCI in 63% of included cases) was performed in 3349 of 8583 patients (39%). In propensity-adjusted multivariable analysis, IVUS guidance was associated with reduced rates of definite or probable stent thrombosis (adjusted HR 0.40; 95% CI 0.21–0.73; $P = 0.003$), myocardial infarction (adjusted HR 0.66; 95% CI 0.49–0.88; $P = 0.004$), and MACE (adjusted HR 0.70; 95% CI 0.55–0.88; $P = 0.003$) at 1 year. Notable limitations of this study were the lack of randomization and lack of pre-specified guidelines for performing and acting on IVUS findings.

In addition to conventional grey-scale IVUS, other ultrasound-based techniques have been used to provide additional diagnostic insights. Assessment of plaque composition may be further improved by analysis of the complete radiofrequency signal using different diagnostic algorithms, including those used in 'virtual histology'.

### 17.2.2 Optical coherence tomography

Optical coherence tomography is a light-based modality of intravascular imaging with higher spatial resolution than IVUS (15 vs. 150 μm) and is ideally suited to accurate detection of intraluminal structures. Plaque composition, including the presence of lipid pools and intraluminal thrombi, can also be determined.[707] Notably, this is the only technique capable of providing accurate measurements of the thickness of the fibrous cap and to detect even minor cap disruptions.[707,708] Early stages of cardiac allograft vasculopathy are frequently angiographically silent, yet can be visualized with OCT or IVUS and are associated with important prognostic implications.[708] Optical coherence tomography requires complete blood clearance from the lumen for imaging, has a limited penetration on the vessel wall and is therefore unable to assess the complete plaque burden. After stent implantation, OCT is more accurate than IVUS in detecting subtle morphological details including malapposition, residual thrombus, plaque prolapse, and residual dissections, although the clinical significance of these findings remains to be determined.[709,710] During longitudinal follow-up investigations, OCT is more accurate than IVUS for assessing even neointimal thickness, strut apposition, and coverage. These findings are important surrogate markers of the efficacy and safety of DES and are frequently used to compare new DES. A recent retrospective and observational study suggested that OCT-guided stenting might improve clinical outcomes.[711] Owing to its very high resolution, OCT is used to reveal the underlying mechanisms in patients with stent failure, including in-stent restenosis and stent thrombosis.[516] Likewise, intrastent neointimal tissue may be characterized, including the detection of