Comments on the 2014 ESC/EACTS Guidelines on Myocardial Revascularization

Comentarios a la guía de práctica clínica de la ESC/EACTS 2014 sobre revascularización miocárdica

INTRODUCTION

The European Society of Cardiology (ESC) guidelines are endorsed by the Spanish Society of Cardiology (Sociedad Española de Cardiología) and translated into Spanish for their publication in Revista Española de Cardiología. In accordance with the policy introduced in 2011, the new guidelines are accompanied by a commentary article that observes the objectives and recommended methodology described by the Guidelines Committee of the Spanish Society of Cardiology.

In the present article, we discuss the new guidelines on myocardial revascularization. The Guidelines Committee formed a working group composed of members proposed by the Spanish Society of Cardiology and the Spanish Society of Thoracic and Cardiovascular Surgery (Sociedad Española de Cirugía Torácica y Cardiovascular). These new guidelines modify previous recommendations and establish new recommendations on the 2 forms of coronary revascularization. To facilitate comprehension of the article, we have summarized the most novel (Table 1) and most contentious (Table 2) aspects in 2 tables.

The guidelines provide an extensive review of clinical trials comparing coronary artery bypass grafting (CABG) surgery and percutaneous coronary intervention (PCI) and are accompanied by a meta-analysis of 100 clinical trials and 93,553 patients. However, in a considerable number of patients, the final decision should be individualized and reached through multidisciplinary interaction among the clinical cardiologist, interventional cardiologist, and cardiac surgeon (heart team or classic medical-surgical conference).

STRATIFICATION AND RISK SCALES

Various scales have been developed for stratifying risk and determining revascularization need and optimum technique. Some focus on surgical risk, such as those of the EuroSCORE (European System for Cardiac Operative Risk Evaluation) and the STS (Society of Thoracic Surgeons), whereas others use angiographic findings to choose between PCI and CABG (SYNTAX; SYNTAX II includes clinical variables). None consider geriatric syndromes, particularly frailty. For the first time, the guidelines discourage the use of EuroSCORE, because it overestimates mortality, with preference being given to EuroSCORE II. The SYNTAX scale appears to be a very valid tool for helping interventionists and surgeons to determine the optimal revascularization type.

CLINICAL DECISION AND PATIENT INFORMATION

The guidelines stress the need to provide patients with sufficient information on the risk/benefit of revascularization. A new development is the recommendation of certain deadlines for percutaneous revascularization or surgery: 2 weeks in patients with angina class 3 with high-risk anatomy or ventricular dysfunction, and up to 6 weeks in the remaining patients with stable disease.

The strengthening of the role of the heart team is very relevant in Spain, where the number of CABGs is noticeably lower than in other countries. The proposal of maximum recommended periods for revascularization could have important repercussions for patient care, given the waiting lists for CABG in many Spanish hospitals.

FUNCTIONAL AND IMAGING TESTS

The guidelines indicate that noninvasive tests should be chosen based on their availability and the experience of each hospital. Special attention is given to the value of fractional flow reserve for analyzing the functional impact of intermediate lesions, and the guidelines support the decision for revascularization when the fractional flow reserve is < 0.80. No mention is made of intravascular ultrasound or optical coherence tomography for identifying significant stenoses requiring revascularization. Moreover, no differences are indicated among the various techniques for evaluating myocardial viability.

REVASCULARIZATION IN STABLE CORONARY ARTERY DISEASE

Coinciding with the publication of the guidelines, the authors have published a network meta-analysis that used indirect comparisons to evaluate the different revascularization strategies of multiple randomized studies. Notably, CABG was associated with a significantly reduced mortality, rate of infarctions, and need for repeat revascularization. The benefits of PCI are only seen in patients treated with new-generation drug-eluting stents (DESs). Compared with medical treatment, there is a gradient of benefit in the need for...
Table 1
Most Novel or Relevant Aspects of the Guidelines on Myocardial Revascularization 2014

| Risk scales | Decisive role of the Heart Team |
| - EuroSCORE use is discouraged. Recommended are the EuroSCORE II and STS and SYNTAX scale (for choosing between CABG or PCI) |

| Clinical decision | Revascularization deadlines are recommended |
| - Fractional flow reserve for analyzing the functional impact of intermediate lesions |

| Functional tests | Revascularization in stable coronary artery disease |
| - The 2 strategies are complementary |
| - In patients with main coronary artery disease: |
| | With favorable anatomy (SYNTAX ≤ 22), same level (I-B) |
| | With complex anatomy (SYNTAX 23-32), I-B for surgery and IIa-B for PCI |
| | With very complex anatomy (SYNTAX > 32), I-B for surgery and PCI is discouraged (III-B) |
| - In patients with 3-vessel disease: |
| | With favorable anatomy for PCI (SYNTAX ≤ 22), I-A for surgery and I-B for PCI |
| | With complex or very complex anatomy (SYNTAX > 22), I-A for surgery and III-B for PCI |

| Technical aspects of surgical revascularization | Revascularization in patients with NSTEACS: |
| - Use of bilateral internal mammary arteries, removed in a skeletonized manner |
| - The radial artery is considered an intermediate graft between mammary artery and venous grafts |

| Technical aspects of percutaneous revascularization | Revascularization in patients with STEMI |
| - Second-generation DESs over conventional stents in all settings. Clinical use of bioresorbable devices when several randomized studies become available |
| | For stent restenosis, a DES or DE balloon is recommended |
| | IVUS if useful in PCI of the left main coronary artery and for stent thrombosis or restenosis |
| | Medina classification for characterization of bifurcation lesions |

| Antithrombotic treatment | Relationship between results and intervention volume |
| - Loading clopidogrel dose of 600 mg in stable patients before they undergo PCI |
| - In patients with NSTEACS, prasugrel use is discouraged before the coronary angiography |
| - In PPCLI, FCP-administered prasugrel or ticagrelor is recommended over clopidogrel. Bivalirudin dropped from a class I recommendation to a class IIa |
| - In patients requiring oral anticoagulation and undergoing PCI, latest-generation DESs are preferred to BMSs |

| Patients who require reintervention or valve intervention | BMS, bare-metal stent; CABG, coronary artery bypass grafting; DE, drug-eluting; DES, drug-eluting stent; FCP, first contact physician; IVUS, intravascular ultrasound; NSTEACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; PPCLI, primary percutaneous coronary intervention; STEMI, ST-segment elevation acute myocardial infarction. |
repeat revascularization: the most effective treatment is surgery, followed by new-generation DESs and conventional bare-metal stents (BMSs). Regarding the results of percutaneous revascularization, solid evidence indicates that new-generation DESs are safer and more effective than BMSs and first-generation DESs.

The new guidelines update the indications for PCI and CABG but insist that both are complementary and always overlap with medical treatment. The mortality benefit of surgery compared with medical treatment is consistent in various studies and is higher in patients with more severe symptoms or ventricular dysfunction.

In patients with involvement of the proximal anterior descending artery, multiple studies and meta-analyses show good results with CABG and PCI without differences in death, infarction, or stroke, although with a greater need for revascularization during follow-up after percutaneous treatment. Notably, most studies were performed before the introduction of the new-generation DESs. Similarly, rates of mammary artery grafting in surgical arms were clearly lower than current rates.

Regarding revascularization of lesions of the left main coronary artery, various randomized studies, predefined subanalyses, and 2 recent meta-analyses\(^5\) suggest that the 2 revascularization types exhibit similar results of total mortality, cardiovascular mortality, and myocardial infarction. Moreover, although CABG increased stroke risk, PCI was associated with a greater need for revascularization during follow-up. Longer-term results indicate that the evidence in favor of surgery is more robust.

According to the new guidelines, in patients with left main coronary artery disease with favorable anatomy (SYNTAX ≤ 22), the recommendation is similar for CABG and PCI (I-B). In patients with moderate anatomical complexity (SYNTAX 23–32), the recommendation is I-B for surgery and IIA-B for PCI. In patients with left main coronary artery disease and very complex coronary artery anatomy (SYNTAX > 32), surgery (I-B) should clearly be recommended over PCI (III-B).

In the prespecified subgroup of patients with 3- vessel disease of the SYNTAX trial,\(^6\) surgery significantly reduced mortality, the rate of infarctions, and the need for repeat revascularization compared with PCI. However, in the SYNTAX ≤ 22 subgroup, the main end point of the study was similar with the 2 approaches. In this regard, although the guidelines give a similar indication, they recognize the greater evidence supporting surgery in patients with 3- vessel disease and a low SYNTAX score (I-A vs I-B).

Several of the new recommendations of the guidelines are based on various conclusions of the SYNTAX trial.\(^7\) Importantly, however, in this study, the main hypothesis of noninferiority of percutaneous revascularization vs surgery was not achieved and patients were not prestratified with the SYNTAX scale before being randomized. Thus, the subgroup analysis conclusions are only hypothesis generators and should be supported by new randomized studies.

### REVASCULARIZATION IN PATIENTS WITH NON–ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME

Early stratification is emphasized to identify patients whose prognosis would be improved by an invasive approach. Patients at highest risk (revascularization in < 2 hours) are those with refractory angina, cardiogenic shock, severe heart failure, hemodynamic instability, or malignant ventricular arrhythmias (I-C). In addition, patients are considered at elevated risk (angiography in < 24 hours, I-A) when they meet one of the following criteria: dynamic electrocardiogram changes, a relevant change in markers (troponin), or a GRADE (Global Registry of Acute Coronary Events) score\(^8\) > 140. In patients with a GRADE score < 140 but with another secondary risk factor, invasive evaluation should be carried out in the first 72 hours (I-A). In low-risk patients without recurrent symptoms, a noninvasive evaluation of inducible ischemia should be performed before a decision is made on the need for coronary angiography (I-A).

No specific study has been made of the optimum type of revascularization in patients with non–ST-segment elevation acute coronary syndrome. The decision is clear in single- vessel disease or when the culprit lesion is easily identified. For PCI, second-generation DESs are recommended over conventional stents (I-A). For patients with multivessel disease without clear identification of a culprit lesion, the decision should be made by the heart team (I-C). For this approach, the use of the SYNTAX scale is highly recommended (I-C), with the application of the same criteria as in patients with stable coronary artery disease.\(^9\) Surgery should be immediately performed in surgical patients with recurrent ischemia, hemodynamic instability, or ventricular arrhythmias. In more stable patients but with left main or 3-vessel disease involving the proximal descending anterior artery, surgery should be performed during hospital admission and dual antiplatelet therapy is only a relative contraindication.

### REVASCULARIZATION IN PATIENTS WITH ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME

New infarction networks are requested to deliver the appropriate reperfusion therapy to most patients (I-A). A door-to-balloon time of < 60 minutes and a first-medical-contact-to-balloon time of < 90 minutes are recommended for patients presenting to a primary...
PCI (PPCI) center. A first-hospital-door-to-balloon time of < 120 minutes is advocated for patients who present to a non–PPCI-capable center or who are collected by the emergency medical service. In addition, the so-called door-in to door-out time was established, which measures the time from when patients arrive to such a center or are attended by the emergency medical service until they are transferred to a PPCI-capable center. This time should be < 30 minutes. The fibrinolysis or PCI should be completed within the time marked by the combination of the 2 variables (first-medical-contact-to-balloon < 120 minutes and door-in to door-out < 30 minutes). If fibrinolysis is to be performed, patients should be immediately transferred to a PCI center. A rescue angioplasty should be performed if the fibrinolysis is unsuccessful; otherwise, an elective coronary angiography should follow after 3 to 24 hours.

In the setting of PPCI and multivessel disease, the recommended strategy is to either treat all serious stenoses during the initial procedure or only that responsible for the infarction. A higher level of recommendation is given to sole treatment of the culprit stenosis and later treatment (days-weeks) of the other stenoses (IIa-B) than performance of a complete revascularization of all lesions contemporaneously with the PPCI (IIb-B). The latest trials support PCI of the other lesions during the initial hospitalization. It remains to be clarified how nonculprit infarct lesions should be evaluated (eg, noninvasive tests, angiography, fractional flow reserve).

Another update to the technique indicates a preference for radial over femoral access (IIa-A) and downgrading of routine use of thrombus aspiration (IIb-A) based on the initial and 1-year results of the TASTE (Thrombus Aspiration during PCI in Acute Myocardial Infarction) trial.14 This latter study has been suggested to include a low-risk population and consequently selective use of thrombus aspiration is recommended to improve coronary artery flow and prevent stent thrombosis. The guidelines propose the use of the new DESS over BMSs (I-A), based on the results of various studies.15,16 Finally, the possible beneficial effect is mentioned of early treatment with intravenous metoprolol for reducing infarct size.17

The indications for coronary surgery in the setting of ST-segment elevation acute myocardial infarction continue to be restricted to patients in cardiogenic shock with anatomy unsuitable for PCI or to patients with mechanical infarct complications. If allowed by the patient’s clinical status, the intervention should be delayed to between 3 and 7 days after the infarction.

REVASCULARIZATION IN PATIENTS WITH HEART FAILURE AND CARDIOGENIC SHOCK

The guidelines recommend CABG in patients with ischemic heart disease and severe left ventricle dysfunction if there is left main coronary artery disease or equivalent (I-C recommendation) and in patients with multivessel disease and stenosis of the left anterior descending artery (I-B). Despite the results of the substudy of the STICH (Surgical Treatment for Ischemic Heart Failure) trial,18 the guidelines continue to recommend revascularization in patients with significant myocardial viability, preferably via surgery (IIa-B) or PCI (IIb-C).

The biggest development in this area is that, as a consequence of the IABP-SHOCK II (Intra-aortic Balloon Pump in Cardiogenic Shock) trial,19 the routine use of intra-aortic balloon pump is discouraged in patients with ST-segment elevation acute myocardial infarction and cardiogenic shock (III-A), except if there are mechanical complications (IIa-C). Short-term mechanical circulatory support may still be used (IIb-C). The downgrading of the use of intra-aortic balloon pumps is radical (from I-C to III-A), given that some methodological aspects of the IABP-SHOCK II trial19 have been controversial. The balloon pump will probably continue to play a role in selected patients with cardiogenic shock due to left ventricular dysfunction.

The downgrading of the use of the intra-aortic balloon pump in patients with shock could have a considerable impact because it is the most used circulatory support system in Spain.

REVASCULARIZATION IN PATIENTS WITH DIABETES

In stable coronary artery disease, revascularization of diabetic patients with documented ischemia and multivessel disease has an I-B indication. Regarding the type of revascularization (CABG or PCI), surgery is clearly recommended over PCI (I-A) in diabetic multivessel disease patients with an acceptable surgical risk. This recommendation is based on the results of the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus) study,19 a subgroup of diabetic patients of the SYNTAX trial,20 and a meta-analysis.21 There is a IIa-B indication for PCI as an alternative to surgery in patients with less severe disease, based on the results of various studies that failed to find differences during follow-up between the 2 types of revascularization in the subgroup of diabetic patients with SYNTAX ≤ 22.

Once the type of revascularization has been selected and, if PCI is chosen, DESs are clearly recommended (I-A). For surgery, the use of mammary artery grafts has a IIa-B indication. Finally, due to the risk of lactic acidosis, renal function should be monitored in diabetic patients on metformin who require coronary angiography or PCI (I-C).

REVASCULARIZATION IN PATIENTS REQUIRING VALVE INTERVENTION

In patients with valve intervention as the primary indication, the guidelines define when routine coronary angiography should be performed before the surgery but introduce the innovation that a noninvasive coronary angiography suffices. The combined procedure is recommended in patients with significant associated ischemic heart disease. In patients with CABG as the primary indication, the guidelines suggest also performing mitral valve repair in patients with severe ventricular dysfunction and moderate or severe mitral regurgitation or to additionally replace the aortic valve in patients with moderate aortic stenosis.

PATIENTS WITH CAROTID ARTERY DISEASE OR ASSOCIATED PERIPHERAL ARTERY DISEASE

The guidelines recommend preoperative computed tomography and intraoperative epiaortic Doppler ultrasound. The document neglects to establish which specific situations demand thoracic computed tomography. There is currently contradictory evidence regarding off-pump surgery and the prevalence of stroke, because various randomized studies have failed to show differences in stroke reduction between surgery with and without extracorporeal circulation. Understandably, patients with highly calcified aortas or at high risk could benefit from off-pump surgery. A IIa recommendation has been established for the use of carotid Doppler ultrasound in patients with multivessel coronary artery disease, peripheral vascular disease, and age > 70 years. The recommendations on carotid artery revascularization in patients requiring CABG depend on the presence or absence of stroke/transient ischemic attack in the 6 months prior to the intervention.

REINTERVENTION AND HYBRID PROCEDURES

For management of acute graft failure, percutaneous treatment is preferable if possible; surgical reintervention should be reserved as the second option. A development is information on the 10-year patency rates for bypasses with the internal mammary artery (95%) and the radial artery (63%-83%). The patency percentages are also reported of the other grafts over time.
Regarding late graft failure, the technique of choice continues to be PCI, and surgery is reserved for patients with diffuse disease, ventricular dysfunction, and absence of patent arterial grafts. There is a tendency for increased use of arterial grafts in cardiac surgery.31 In the percutaneous management of venous graft lesions, DESs seem to provide better results than BMSs.

The guidelines mention the possibility that some centers performing the PCI may lack a cardiac surgery team. This aspect could have care-related implications if highly complex procedures are performed without an on-site cardiac surgery team. Hybrid procedures with valve surgery and elective PCI that treat the valve disease via minimally-invasive surgery and perform percutaneous revascularization when the lesions are amenable to intervention are suitable options in high-risk patients.

ARRHYTHMIAS

New recommendations include immediate coronary angiography and revascularization of all survivors of an out-of-hospital cardiac arrest (IIa-B) or patients with electrical storm (IIa-C) if there is no clear noncoronary cause of the arrhythmia. Regarding primary prevention, the guidelines continue to support ischemia assessment with eventual revascularization in coronary patients with severe ventricular dysfunction prior to defibrillator implantation (IIa-B). Anticoagulation therapy is recommended for at least 3 months in patients who have had an episode of atrial fibrillation after surgical revascularization (IIa-C), as well as anticoagulants for patients with paroxysmal atrial fibrillation after percutaneous revascularization (IIa-C). Oclusion or removal of the left atrial appendage is considered acceptable (IIb-C) during surgery of atrial fibrillation patients, as well as PCI-associated percutaneous closure in atrial fibrillation patients with a contraindication for combined treatment with anticoagulants and antiplatelet agents (IIb-B).

TECHNICAL ASPECTS OF SURGICAL REvascularization

Regarding the preoperative management of CAGB, no withdrawal of previous medication is recommended, except for angiotensin-converting enzyme inhibitors 1–2 days before the procedure. Blood transfusions and preoperative anemia have been associated with greater perioperative morbidity and mortality.

Also recommended is endoscopic vein harvesting (IIa), as well as the use of the bilateral internal mammary artery, ideally obtained via skeletonized dissection. Bilateral internal mammary artery grafting should be used in all patients <70 years or whose life expectancy exceeds 5 years. The benefit-risk ratio should be evaluated in obese and diabetic patients due to the higher risk of sternal infection entailed by bilateral internal mammary artery grafts. The radial artery remains as an intermediate graft between the mammary artery and venous grafts. Coronary interventions are defined as complete revascularizations when all epicardial vessels with a diameter ≥1.5 mm and lesions with a ≥50% severity are grafted.

TECHNICAL ASPECTS OF PERCUTANEOUS REVAScularization

The guidelines indicate that there is no clinical or anatomical context supporting the use of BMSs over DESs. Neither have BMSs been shown to be superior to DESs in relation to the risk of late thrombosis or in the case of unplanned interruption of antithrombotic therapy. The efficacy and safety of second-generation DESs are clearly higher than those of BMSs and first-generation DESs, both for the treatment of native lesions and those situated in saphenous vessels. The benefit of BMSs in anticoagulated patients is now not supported by the data obtained with the new-generation DESs.

Bioresorbable stents have shown promising results that are similar to those obtained with new-generation DESs in observational studies of patients with simple lesions. However, the guidelines stress that their clinical use can only be established when their efficacy and safety are shown in several randomized studies. Drug-eluting balloons have shown their usefulness in patients with in-stent restenosis within BMSs or DESs. Both the use of a DES and that of a drug-eluting balloon receive a I-A recommendation in these guidelines for patients with in-stent restenosis within BMSs or DESs.

The guidelines indicate that intravascular ultrasound is the best technique for assessing the progression/regression of coronary atherosclerosis and for stent optimization during its implantation (IIa-B). The guidelines particularly recommend the use of intravascular ultrasound during treatment of the left main coronary artery (IIa-B) and also in patients with stent thrombosis or restenosis (IIa-C). The document recognizes the value of optical coherence tomography for determining plaque characteristics, measuring the thickness of the fibrous cap covering the lipid core, and assessing in-stent neoatherosclerosis. This type of tomography is the technique of choice for evaluating the efficacy of new DESs, because neointimal thickness can be determined with great precision.

The guidelines suggest the use of the Medina classification23 for characterizing bifurcation lesions, as well as provisional stenting for their treatment (IIa-A). Treatment of chronic occlusions should be considered in the presence of symptoms or diagnostic data of ischemia or viability (IIa-B).

ANTITHROMBOTIC TREATMENT

The new antithrombotics acquire a prominent role in these guidelines. In patients with stable ischemic heart disease revascularized by PCI, the new guidelines recommend a clopidogrel loading dose of 600 mg, administered at least 2 hours before elective PCI (I-A) or in the catheterization laboratory itself if it has not been administered beforehand. A novel aspect is the reduction of dual antiplatelet therapy to 6 months after DES implantation (I-B). In addition, the guidelines reiterate the need to instruct patients on the importance of adhering to dual antiplatelet therapy after the PCI.

In patients with non-ST-segment elevation acute coronary syndrome revascularized by PCI, the level of recommendation is similar for prasugrel and ticagrelor (I-B), although prasugrel is recommended in patients with known coronary anatomy and established PCI indication. Prasugrel use is discouraged (III-A) before coronary angiography in patients admitted with non–ST-segment elevation acute coronary syndrome. The routine upstream use (prior to coronary angiography) of glycoprotein IIb/IIIa inhibitors (III-B) is discarded. If glycoprotein IIb/IIIa inhibitors are indicated in the catheterization laboratory, such as in bail-out situations or for lesions with a large amount of thrombotic material, abciximab is preferred (IIa-C).

In patients with ST-segment elevation acute myocardial infarction treated with PPCI, the guidelines clearly recommend prasugrel or ticagrelor administration in the first physician contact (I-B). Glycoprotein IIb/IIIa inhibitor use remains confined to the catheterization laboratory (IIa-C). In high-risk patients, there continues to be a weak recommendation (IIb-B) for their upstream use before arrival at the hospital.

In relation to anticoagulation, there has been a notable downgrading in the recommendation level for bivalirudin in PPCI, dropping from I-A to IIa-A, due to the results of the EUROMAX32 and HEAT-PPCI32 studies, which confirm a significant increase in the rates of early stent thrombosis compared with heparin. A new development is the incorporation of bolus intravenous enoxaparin as an anticoagulant for PPCI.

The recommendations in patients revascularized by PCI requiring oral anticoagulants are collected in a new table. Notable is the preference for latest-generation DESs over BMSs in patients requiring oral anticoagulants and with a low risk of bleeding (IIa-C).
Additionally, the use of prasugrel and ticagrelor is discouraged in patients requiring oral anticoagulants (III-C). In elective PCI, there is no need for additional anticoagulation therapy if the INR (international normalized ratio) is > 2.5. In PPCI, parenteral anticoagulation should be administered in patients treated with oral anticoagulants, independently of the period from the last anticoagulant dose (I-C).

**RELATIONSHIP BETWEEN RESULTS AND INTERVENTION VOLUME IN CORONARY REVASCULARIZATION**

The guidelines recommend a minimum annual volume of CABG interventions per hospital of > 200 cases (Ila-C). However, other related factors are not considered, such as the number of interventions per surgeon. In addition, the guidelines recommend routine use of the internal mammary artery (< 90%) and suggest reporting the case data of all departments to national and European registries (I-C). In a similar manner to PCI, the guidelines indicate that the best results are obtained by operators with higher caseloads within larger volume centers. Physicians are recommended to undergo their training in interventional cardiology (1-2 years) in accredited institutions, where the operator performs > 200 interventions as first operator, with more than a third of these cases in patients with acute coronary syndrome. The institutions granting the accreditation should have 24-hour on-call teams and should perform > 800 PCIs per year (IIa-C). In addition, centers with < 400 PCIs per year are recommended to collaborate within organized care networks with higher-volume institutions. Finally, more complex elective interventions should be performed by experienced operators in centers with access to circulatory support and preferably with on-site cardiovascular surgery (Ia-C).

**APPENDIX. Authors and Reviewers**

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**CONFLICTS OF INTERESTS**

None declared.

**REFERENCES**


