ESC/EACTS guidelines on myocardial revascularization post-SYNTAX

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Keywords: Guidelines • Myocardial revascularization • Coronary bypass surgery • Percutaneous coronary intervention • Coronary artery disease

It is befitting that the new ESC/EACTS guidelines have been formulated on the occasion of the 50th anniversary following the performance of the first coronary artery bypass operation in 1964 [1]. Treatment strategies for patients with coronary artery disease (CAD) have undergone the most extensive scrutiny by way of randomized, controlled trials (RCTs), meta-analyses and in-depth evaluation of large registries over the last five decades. Based on the evidence provided by these research tools, guidelines on myocardial revascularization for CAD have been formulated every 4–5 years by selected experts in the field, with the intent of not only assisting cardiologists, cardiac surgeons and physicians of selecting the optimum management strategy for each individual patient, but also of creating educational tools and implementation programmes for the next generation of physicians. More importantly, the guidelines are non-partisan and are exclusively supported by the best available clinical, ethical and technical evidence without economic or industry influence. The 2010 ESC/EACTS guidelines were unique in several aspects [2]. The writing committee, which included a proportionate number of cardiologists and cardiac surgeons for the first time, emphasized the importance of the Multidisciplinary/Heart Team in decision-making in patients with complex stable CAD and communication of appropriate evidence-based information to patients requiring nonemergency interventions. The new 2014 ESC/EACTS guidelines have incorporated these unique and other recommendations with appropriate amendments based on new evidence available since the last edition. They involve a broad systematic overview on all facets of CAD and provide the best possible evidence-based recommendations for diagnostic strategies, risk stratification, treatment policies for simple and complicated CAD with and without associated diseases, complementary therapies like post-procedural medications and secondary prevention. Finally, for the first time, the assessment of the impact of procedural volumes on patient outcomes has led to the creation of recommendations for training, proficiency and operator/institutional competence in CABG and percutaneous coronary intervention (PCI) [3].

Invasive coronary angiography is the diagnostic tool of choice in symptomatic patients, in whom CAD is highly anticipated. In patients with an intermediate probability of disease, noninvasive or functional testing through stress echocardiography, nuclear imaging, stress magnetic resonance imaging or positron emission tomography is initially recommended, followed by invasive angiography if needed. Once the decision to perform revascularization has been made, risk stratification and the optimal timing and mode of revascularization have to be established, the latter being potentially the most debated topic due to rapid technological advancements in CABG and PCI.

Optimal timing and mode of revascularization have always played an important role in achieving satisfactory outcomes in patients with acute coronary syndrome and cardiogenic shock. Primary PCI of the culprit vessel within 12 h from symptom onset with new-generation drug-eluting stents (DES) continues to remain the treatment of choice in patients with ST-elevation myocardial infarction (STEMI). In patients presenting later, primary PCI should be performed in case of ongoing ischaemia, life-threatening arrhythmias or chest pain. CABG is only reserved for candidates not amenable to PCI or at the time of repair of mechanical complications of STEMI. In patients with non-STEMI, an early invasive strategy is recommended for high-risk patients (rising cardiac enzymes, dynamic ST- or T-wave changes, poor left ventricular function etc.) with the choice of revascularization therapy according to a predefined Heart Team protocol based on clinical status, comorbidities and anatomical severity of CAD. Acute coronary syndrome complicated by cardiogenic shock due to left ventricular failure should be revascularized (preferably by PCI) emergently with periprocedural support of short-term mechanical circulatory assist devices in haemodynamically unstable patients. Routine use of intra-aortic balloon (IABP) support, which was a level I recommendation in these patients according to previous guidelines, has been disapproved in the current version [3], because of failure of the IABP-SHOCK II trial to prove its efficacy [4].

A new feature, in the current guidelines, is the recommendation of a time-line of 2 weeks for revascularization of highly symptomatic patients (Canadian Cardiovascular Society class 3) with stable, but anatomically high-risk multivessel CAD [MVCAD: left main (LMD) or equivalent, three-vessel (3VD) or proximal left anterior descending artery (LAD) disease] and 6 weeks for all other patients once the decision of revascularization has been made. This could potentially avoid the occurrence of untoward events in patients awaiting revascularization. However, this should not be used as a rationale for unrestricted performance of ad hoc PCI, the indications of which should be clearly outlined in institutional protocols formulated by the Heart Team in accordance with current guidelines. Several risk stratification models have been developed to evaluate
the risk/benefit ratio of revascularization procedures for this patient group, so that the safest and most efficacious revascularization strategy can be selected. As physicians and surgeons are ready to treat more complex and challenging patients with increasing age, comorbidities, frailty and multiple previous cardiac procedures reflecting the tremendous improvement in periprocedural medications and intensive care unit care, newer models for risk stratification have been developed. The EuroSCORE II, which is a derivative of more current datasets and may have a better ability to predict early mortality after CABG, has replaced the EuroSCORE in the 2014 guidelines as the latter was shown to overestimate the risk of mortality [5]. Additionally, use of models like the logistic clinical SYNTAX score [6] and the SYNTAX score II [7], which have been developed by amalgamating the anatomical SYNTAX score with clinical variables, has been recommended by the new guidelines to assess medium- to long-term outcomes after PCI and to provide a personalized approach to decision-making between CABG and PCI, respectively.

The risk/benefit ratio remains the focal point of decision-making during selection of a revascularization procedure for a patient with stable CAD. Interventional cardiologists need to be aware of the fact that most RCTs and meta-analyses have been unable to prove a significant benefit of PCI over optimal medical therapy (OMT) with regard to survival and freedom from myocardial infarction (MI). Hence, the current guidelines continue to recommend OMT as the first line of treatment in these patients. Nevertheless, revascularization, especially with CABG, does provide a prognostic benefit in specific patient subsets such as those with significant LMD or proximal LAD disease, two-vessel disease or 3VD with left ventricular (LV) dysfunction, large myocardial area at risk (>10%) and single patent coronary artery with >50% stenosis, in addition to symptomatic relief in patients with refractory angina, thus improving exercise tolerance and quality of life. OMT should always be considered complimentary to revascularization rather than its competitor.

The most controversial topic over the last three decades has been the choice of revascularization therapy for patients with stable MVCAD. Although PCI was accepted as a comparable choice to CABG in the treatment of patients with one- or two-vessel disease without the involvement of the proximal LAD, it was still not equivalent to CABG for the proximal LAD and MVCAD. As per the 10-year results of the RCT between PCI with bare-metal stents and minimally invasive direct coronary artery bypass surgery [8], which showed no difference in major adverse cardiac events, the current guidelines have upgraded the use of PCI for single- and double-vessel CAD with proximal LAD stenosis to level I. Nonetheless, it is vital that the patients be informed by interventionists about the significantly higher rate of target vessel repeat revascularization (34 vs 11%; P = 0.01) with PCI than with surgery [8]. Numerous RCTs conducted in the late 1990s and the first decade of this century comparing CABG with PCI in patients with MVCAD could not demonstrate a significant difference between the two modes of therapy with regard to survival or freedom from MI [9, 10]. This was chiefly attributed to the fact that most of these trials recruited low-risk patients, in whom surgery would anyway provide no prognostic benefit and included <10% of the patients screened, thus not representative of patients encountered in real-world practice. Nevertheless, meta-analyses and reports from large registries which truly characterize the real-world scenario portrayed a completely different picture with a major advantage in favour of CABG with regard to survival, MI and repeat revascularization (RR) [11, 12]. Additionally, with the introduction and more prevalent off-label use of first-generation DESs, which were associated with lower restenosis rates at the cost of safety due to stent thrombosis, and the progress in CABG techniques (off-pump CABG and total arterial revascularization), it became pertinent to compare the contemporary techniques of PCI and CABG in patients with stable MVCAD. This fact chiefly helped conceptualize the SYNTAX trial, in which consecutive patients (n = 3075) with complex MVCAD (de novo 3VD or LMD) who were suitable to undergo treatment by both CABG and PCI with the first-generation paclitaxel-eluting stents were enrolled in the Trial (n = 1800) and those who were deemed appropriate only for one treatment or the other were enrolled in a nested registry (n = 1275), so that even patients not included in the trial were captured. Thus, more than two-thirds of the patients (n = 3075, 71%) screened were recruited, either in the randomized (n = 1800) group, when eligible, or in the PCI- and CABG-nested registries (n = 1275) [13]. This trial was responsible in bringing about major alterations in the last version of the guidelines on myocardial revascularization with the introduction of the Heart Team concept and the utilization of the SYNTAX score in decision-making with regard to the choice of revascularization therapy. The recently published 5-year results of the Trial [14] and its various prespecified subgroups [15–17] have led to further alterations in the current guidelines, so much so that, for the first time, the recommendations have been explicitly classified according to the type of disease, i.e. 3VD or LMD and the three SYNTAX score terciles.

In patients with 3VD, not only was the occurrence of major adverse cardiac and cerebrovascular events (MACCEs), composite safety end-point of death/stroke/MI, and RR significantly higher after PCI than CABG, but also MI, cardiac and all-cause mortality rates were significantly greater after PCI with broadening of the gap with passage of time from the procedure [15]. Furthermore, PCI was also found to independently predict MACCEs, all-cause mortality and the composite end-point of death/stroke/MI. However, an analysis of outcomes based on the SYNTAX score terciles revealed that there was no difference in outcomes between PCI and CABG in patients with low SYNTAX scores. However, with increasing complexity CABG performed significantly better than PCI. Hence, the current guidelines have upgraded the use of PCI for 3VD with SYNTAX score <22 to level I. For 3VD with SYNTAX scores >22, CABG remains, undisputedly, the treatment of choice. Patients with LMD showed no difference in the rates of MACCEs, composite end-point of death/stroke/MI, all-cause or cardiac death and MI [16] with regard to the mode of revascularization. Nonetheless, CABG was associated with a significantly greater stroke risk than PCI, whereas the reverse was true for RR rates. This so-called trade-off should be clearly explained to the patients as the implications of each are quite different. Similar to 3VD, complexity of disease did affect outcomes. Only patients with high SYNTAX scores benefitted from CABG. Thus, the current guidelines recommend comparable use of PCI for LMD with SYNTAX scores <22. For intermediate SYNTAX scores PCI is a good alternative, but patients with SYNTAX scores >33 should be treated with CABG. Diabetic patients undergoing CABG in the SYNTAX trial benefitted immensely in the long term with respect to MACCE and RR rates, with worse outcomes for PCI in insulin-dependent diabetics [17]. This was further corroborated by the FREEDOM trial, which reported a significantly higher incidence of the composite end-point of death/stroke/MI in PCI-treated than CABG-treated patients, but was chiefly driven by significant differences in MI and all-cause mortality [18]. Hence, the current guidelines have upgraded the use of CABG in diabetic patients with stable MVCAD with an acceptable surgical risk to level I.
Even though the appropriate revascularization strategy forms the focal point of predicting outcomes in patients with CAD, there are several ancillary factors that also significantly affect outcomes. The results of PCI would be expected to improve with every new generation of stents with regard to restenosis and stent thrombosis. Correspondingly, use of state-of-the-art surgical techniques recommended in the current guidelines, such as total arterial revascularization with bilateral skeletonized internal mammary arteries would not only further reduce the need for RR, but also improve extended long-term survival (20–30 years), a time-frame that has never been estimated or evaluated for PCI. Regular use of off-pump surgery without aortic manipulation, with aggressive and judicious use of antiplatelet medications especially in patients with atherosclerotic disease of the ascending aorta would help reduce, if not eliminate, the main problem of stroke noticed early after CABG. Adjudication or referral of patients to high-volume centres and surgeons would further improve the quality of both PCI and CABG, which would translate into excellent outcomes for our patients. The current guidelines have, for the first time, included recommendations on the minimum number of cases to be performed by trainees before becoming independent and by operators to be able to perform PCI for specific subsets. Additionally, the use of physiological revascularization as guided by the fractional flow reserve would probably further improve the efficacy and safety of revascularization. Lastly, hybrid procedures, which involve consecutive or simultaneous surgical and interventional revascularization might provide an excellent solution in specific patient subsets, but should be restricted to high-volume experienced centres.

Although the guidelines are diligently formulated by the experts in the field of CAD after an in-depth search of the literature, their goal would be achieved only if earnestly put into practice by the cardiovascular society as a whole. While the final choice of therapy remains with the patients, it is largely dependent on the information provided to them by the cardiologists, who remain the so-called gatekeepers for patients with CAD. For example patients should be informed that despite the evolution in stent technology, when compared with CABG, restenosis within the target lesion or vessel continues to remain the Achilles heel of PCI. This necessitates one or more reinterventions, entailing repeated admissions to the hospital with the potential of developing complications with every reintervention. In the ideal world, every patient requiring revascularization should have the opportunity of consulting a cardiologist and a cardiac surgeon to acquire an unbiased opinion. However, this is not always possible due to logistical reasons, especially in remote hospitals, where cardiac surgical facilities are not available. It would be advisable that such centres develop treatment protocols based on the guidelines, enabling appropriate management in a majority of the patients. For a small number of patients who require an individualized treatment plan, cardiac surgical colleagues in referral hospitals could be consulted. Our fundamental philosophy as physicians should be patient-centric and not treatment-centric, because finally, our main objective should be to improve the health of our patients in the safest and most efficacious way possible.


REFERENCES