**INVITED ARTICLE**

# Revascularization treatment in patients with coronary artery disease

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**Abstract**

The choice of optimal revascularization strategy in patients with coronary artery disease (CAD) is becoming more challenging lately, due to recent advances in percutaneous coronary intervention (PCI) and coronary artery bypass grafting surgery (CABG). On one hand, drug-eluting stents (DES) have emerged as a solution to the problem of restenosis after balloon angioplasty or bare-metal stent implantation, which was responsible for a higher rate of events (mainly repeat revascularization) in relation to CABG. On the other hand, off-pump bypass techniques and minimally invasive grafting of the left anterior descending artery appear to be safe and efficacious alternatives to traditional, on-pump CABG. Available literature includes studies outdated by current technologies, leaving the dilemma of best revascularization strategy unanswered in the general CAD population, but also in high-risk groups, such as diabetics and patients with chronic kidney disease. A number of ongoing trials, especially designed for this purpose, are set to end the debate, providing head-to-head comparisons between DES-assisted PCI and contemporary bypass surgery. Hippokratia 2008; 12 (1): 3-10

**Keywords:** percutaneous coronary intervention, coronary artery bypass grafting, drug-eluting stents, off-pump bypass surgery

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As coronary artery disease (CAD) patients increase, so does the need for optimal choice of revascularization strategy, in the setting of both chronic stable angina and acute myocardial infarction. Moreover, the two available modes of coronary revascularization, i.e. percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), demonstrate recent advances, the effectiveness of which, if confirmed in ongoing trials, will change the current landscape in the management of CAD. Of course, it cannot be stressed enough that not all patients with CAD have an indication for revascularization; recommendations for these procedures (implying a benefit over medical therapy alone, in terms of either hard clinical endpoints or symptom control) have been clearly described in recent guidelines[1] and in general include multivessel, left main (MVD and LMD, respectively) and proximal left anterior descending artery (LAD) disease, symptom refractoriness to optimal medication and high risk patient characteristics. Interestingly enough, only CABG –and not PCI- offers a clear survival benefit over medical therapy alone, and this is true in certain patient populations. This article will focus away from this comparison between medical treatment and revascularization procedures and revisit the question: "PCI or CABG?" in multivessel disease, with a special interest on patients with diabetes or chronic kidney disease. A comparison between stent types will be attempted, and advances in the field of bypass surgery discussed. Emphasis will be given to trials currently under way, the results of which may affect clinical practice and help shape future guidelines.

## Multivessel disease

The historical randomized trials of the 1990s that produced the first results regarding the comparison between CABG with percutaneous transluminal coronary baloon angioplasty (PTCA) have long been outdated due to the advents in Interventional Cardiology, mainly the introduction of stents, bare metal (BMS) and drug-eluting (DES) ones, as well as the evolution of surgical techniques, such as arterial graft harvesting, off-pump procedures and minimally invasive approaches. The Randomized Intervention Treatment of Angina trial (RITA-1) included 1011 patients, 45% with single-vessel disease and 55% with MVD, and was the first to demonstrate, both at one-[2] and five-year follow-up[3], a non-significant difference in mortality, myocardial infarction (MI) and total health-care costs between balloon angioplasty and CABG; the latter, however, was associated with fewer anginal symptoms and reinterventions. Another "classic" study was the Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI), which randomized 1054 symptomatic MVD patients to CABG or PTCA; similar one-year mortality was recorded, with more reinterventions and clinically significant angina in the PTCA arm[4]. A more recent analysis of the CABRI data, however, showed that, after adjustment for baseline variables, including CAD angiographic scores, mortality was significantly greater in the PTCA group[5]. The last of the large-scale conventional angioplasty vs CABG trials was the Bypass Angioplasty Revascularization Investigation (BARI), which consisted of a randomized

group (1829 MVD patients equally suitable for CABG and PTCA) and the BARI registry (the remaining 2010 of the patients initially enrolled)[6]. According to the 10-year results that were recently published[7], survival, MI occurrence and angina were comparable in the two arms of the randomized group, while repeat revascularization was higher for PTCA patients. An earlier analysis of the BARI data also demonstrated similar 7-year survival for CABG and PTCA in high-risk anatomic subsets, in which survival is prolonged by CABG versus medical therapy. Finally, the analysis of the BARI registry data revealed a two-times greater preference to PTCA compared to CABG and equivalent 7-year mortality rates[8]. All in all and with the exception of the CABRI reanalysis, the randomized trials of the 1990s agreed on similar mortality and MI rates for balloon angioplasty and CABG, the latter requiring fewer reinterventions during follow-up.

A newer set of trials, with recruitment periods extending from the middle of the last decade to the beginning of the 2000s, attempted to evaluate the effectiveness of the newly applied, uncoated stents versus CABG. Since the inferiority of PTCA versus CABG had been attributed directly to restenosis and the subsequent need for reintervention in previous studies, the introduction of stents, aimed to protect from restenosis, should improve PCI outcomes. The Arterial Revascularization Therapies

Study (ARTS) randomized 1205 patients with MVD to stent implantation or bypass surgery, both modalities being able to revascularize the patient to the same extent. One-year results demonstrated that PCI with stenting had similar rates of death, MI and stroke with CABG, and a lower cost; it necessitated, though, repeat revascularization more often[9]. The Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) trial[10] initially enrolled 2431 patients, who were divided into

stent thrombosis; however, the number of participants was significantly lower than in the afore-mentioned studies[62]. As for PES, the PASSION trial showed only a trend towards PES superiority over BMS in MACE and TLR[58]. It has to be pointed out that these studies report short-term outcomes (maximum 1 year), and the possibility exists that cases of really late stent thrombosis might have been lost. The only long-term reports available come from two related dutch registries, the RESEARCH and the T-RESEARCH registries[59], where 3-year outcomes after SES, PES or BMS implantation are recorded: only a trend towards fewer events was found in favour of SES over BMS, with thrombosis rates being higher in the SES and PES arms, although not at a statistically significant level. All above data considered together, suggest that DES are quite safe and effective in treating coronary lesions in stable patients with CAD or in the setting of primary PCI for STEMI. Fine differences between agents used in stent coating and the issue of stent thrombosis remain to be elucidated by trials to come.

**Advances in coronary artery bypass surgery**

In parallel to the developments in percutaneous coronary interventions, bypass surgery has recently demonstrated its own advances that challenge the traditional on-pump coronary bypass surgery (ONCAB) and strengthen the opposition to drug-eluting stents. Off-pump coronary bypass surgery (OPCAB) has been around for years, gaining ground over ONCAB in everyday practice. Head-to-head comparisons of the two techniques have been conducted, either with a prospective design or retrospectively. Several issues have been resolved, while others need to be further investigated. Graft patency following OPCAB has been shown in two meta-analyses of randomized trials to be compromised in relation to ONCAB, suggesting an increased risk of graft occlusion[63,64]; revascularization was also found to be less complete with OPCAB[63]. Regarding mortality rates, the off-pump technique appears at least non-inferior to conventional surgery: in a New York database study, OPCAB demonstrated lower in-hospital and similar 3-year mortality with ONCAB[65], confirming an older finding of better mortality rates in high-risk patients with multi-vessel disease[66]. As for the need for reinterventions, it has been found to be higher after OPCAB[65], but not unanimously[67]. Quality of life, as perceived by patients after bypass surgery, seems to be higher in the OPCAB groups[67,68], while at the same time costs are kept lower than in conventional surgery[67]. Perioperative risk is lower for OPCAB, with fewer blood transfusions, less myocardial necrosis, less neurocognitive deficit, and, perhaps most importantly, better preservation of renal function, either in patients with pre-existing diabetic nephropathy[69] or in dialysis patients[70]. Conclusively, both surgical techniques seem to offer an excellent outcome to patients referred for surgical revascularization. Off-pump surgery has a more favourable perioperative profile and offers comparable survival with conventional CABG, but is also characterized by a lower graft patency rate, which is translated into a more frequent need for repeat revascularization.

Totally endoscopic coronary artery bypass (TECAB) of the left anterior descending artery (LAD) with thoracoscopic harvesting of the left internal mammary artery (LIMA) has been already implemented with success, with low mortality, perioperative morbidity and satisfactory LIMA patency[71,72]. It was initially intended for isolated high-grade stenosis of proximal LAD. In this setting, a meta-analysis comparing TECAB to bare-metal stenting was performed, demonstrating similar mortality and MI rates, but less TVR with TECAB[73]; however, the only trial with DES was excluded from the analysis. Based on the efficacy of this novel, minimally invasive surgical technique, integrated coronary revascularization has been proposed: it combines TECAB to LAD with DES implantation to the non-LAD lesions. Experience is growing, even in high-risk groups, such as diabetic patients[74], and sufficient data exist to justify a randomized comparison of this integrated approach with traditional CABG. Still, optimal timing of PCI in relation to TECAB has to be found and a higher than usual reintervention rate for lesions corrected with stenting needs to be explained[72].

**Conclusions**

Revascularization procedures in CAD patients who are truly in need of them (as medical therapy alone is sometimes as effective) have evolved significantly, making comparisons more difficult than they were in the era of balloon angioplasty without stenting, when bypass surgery was undoubtedly superior to PTCA in all aspects. The introduction of bare-metal stents closed the gap with CABG, and the addition of DES strengthened the argument for PCI. Mortality and recurrent MI rates do not differ and the higher rate of reinterventions is the cost a patient has to pay for the fewer periprocedural events that PCI offers in relation to CABG. Drug-eluting stents are not superior to BMS at all times, and recommendations concerning their use have to be followed, since high health-care costs and longstanding antiplatelet treatment are drawbacks to their unrestricted use; as for stent thrombosis in DES-treated patients, it does not appear now as menacing as it did before. Ongoing and future randomized trials, rather than registries or retrospective studies, will elucidate unresolved issues both in the general CAD population and in high-risk groups, such as diabetic patients.

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