



Minimally invasive surgical techniques in the era of hybrid coronary revascularization: additional benefits for the elderly patients?

Antonio Nenna, Mario Lusini, Salvatore Matteo Greco, Elvio Covino, Massimo Chello*

Department of Cardiovascular Surgery, Università Campus Bio-Medico di Roma, Rome, Italy

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Geriatric patients affected by stable multi-vessel coronary artery disease (CAD) are at the crossroad: they can live with the risks of acute coronary syndrome, malignant arrhythmias or heart failure, or they can undergo a rapid evaluation for myocardial revascularization. It might be a common thought that the risks inherent the revascularization procedure outnumber the perceivable benefits in older patients, and the percutaneous or especially the surgical option tends to be abandoned. Those “high risk” patients are generally discharged with maximum tolerated medical therapy. All over the world, patients with multivessel CAD are becoming older and with a greater number of comorbidities,^[1] and it is important to point out that those patients should not be negated a revascularization procedure, which proved to prolong survival from cardiac-related events.^[2] Appropriate interventions for elderly patients should be delineated shortly, as the number of octogenarians is expected to quadruple in the next 50 years.^[3]

Complete myocardial revascularization (CMR) has been shown to provide a better recovery of ventricular function and protection against adverse ischemic and arrhythmic events, which results into a longer survival and freedom from reintervention.^[3-5] Surgical revascularization using coronary artery bypass graft (CABG) is known to provide a higher proportion of CMR of all diseased myocardial territories, and is generally the treatment of choice in patients with multivessel CAD.^[6,7] Using percutaneous coronary intervention (PCI), several barriers prevents CMR in a real-life scenario: patient-related factors and technical details of the procedure, such as chronic total occlusion.^[8] However, CMR compared with incomplete myocardial revascularization (IMR) is associated with longer duration of surgery and increased procedural risks. Those daunting issues are crucial when considering geriatric patients, and a

tailored approach which allows to achieve a “reasonable incomplete revascularization” was initially proposed as a challenging alternative.^[9-11] Recent PCI and CABG trials suggest that IMR may be an acceptable option in certain circumstances on the basis of the long-term satisfactory outcomes.^[12] On the other hand, IMR predicts long-term mortality and hospital readmission, regardless of age, severity of CAD, clinical presentation of comorbidities. Also, patients who underwent IMR had greater incidence of in-hospital mortality or major postoperative adverse events, including myocardial infarction.^[3,13] Those results strengthen the conclusion of a meta-analysis which suggested that it was the degree of revascularization, rather than the revascularization approach (percutaneous or surgical), was inversely associated with mortality rates.^[8]

In this intricate debate, the ideal treatment would allow to achieve complete revascularization minimizing procedure-associated risks. Surprisingly, this seems to be less utopian than expected. CMR can be achieved using both surgical and percutaneous approaches, striking a balance between them and reducing risks associated with each technique. The major limitation of CMR using CABG is the need of cardiopulmonary bypass, while excessive stent implantation during percutaneous procedures may exacerbate renal failure or increase intraoperative risks. Therefore, it appears reasonable to perform surgery without cardiopulmonary bypass, without the manipulation of the aorta, and minimize the number of implanted stent. This is the rationale for hybrid coronary revascularization (HCR).

HCR is defined as a planned combination of surgical left internal mammary artery (LIMA) to left anterior descending artery (LAD) grafting and percutaneous treatment of at least one non-LAD coronary arteries. HCR can be performed using a single-stage approach, with surgical procedures immediately followed by PCI in a hybrid operating room, or a two-stage approach, with either CABG or PCI first. The

*Correspondence to: m.chello@unicampus.it

optimal timing and the sequence of the procedures still have to be determined, since results from the literature are not definitive.^[14]

In recent years, off-pump techniques affirmed their role in myocardial revascularization. Avoiding the risks associated with cardiopulmonary bypass, aortic manipulation and cardioplegia, beating-heart revascularization resulted in decreased rate of procedural adverse events,^[15] without reducing the graft quality.^[16,17] Off-pump surgery proved to have benefits in terms of perioperative outcomes compared with conventional surgery especially in high risk populations, such as patients with severely impaired ejection fraction or octogenarians.^[18,19] Revascularization of the LAD has been shown to be the most significant prognostic factor among patients with CAD,^[20,21] and IMR with off-pump LIMA-to-LAD graft has recently has shown better results than optimal medical therapy alone among high risk patients, in terms of survival from all-cause mortality and cardiac-related mortality.^[2] By providing perfusion to the greatest portion of the myocardium, LIMA-to-LAD graft might protect the heart from adverse left ventricular remodeling and reduce proarrhythmogenic foci.^[2,22] The biological processes triggered by the reperfusion of ischemic or stunned segments of myocardium appears to be profoundly different after percutaneous or surgical revascularization, and this may account for greater results after surgical revascularization of the LAD compared with PCI.^[23] Also, arterial grafts have been shown to release a high quantity of nitric oxide, a known inducer of angiogenesis, and this may partially explain the superior outcome of these conduits in myocardial revascularization compared with stent implantation.^[24,25]

HCR using off-pump surgery allows to combine the benefits of a low risk surgical LAD revascularization with the completion of the revascularization using PCI in non-LAD vessels.^[26] This allows to achieve CMR even in elderly patients by means of a succession of two lower-risk procedures rather than with one high-risk procedure.

As in other fields of cardiac surgery in recent years, minimally invasive strategies renovated the interest in the flourishing ground of HCR and are likely to provide additional benefits for the elderly patients with multi-vessel CAD. Revascularization without cardiopulmonary bypass, also known as off-pump CABG, can be combined with non-sternotomic approaches with the aim to minimize invasiveness and reduce intraoperative risks. Left minithoracotomy minimally invasive direct coronary artery bypass (MIDCAB), endoscopically assisted (EACAB), robotically-assisted (RACAB) or totally endoscopic coronary artery bypass (TECAB) have been recently introduced in

current clinical practice across many cardiac surgery centers.^[27] According to the guidelines, HCR using MIDCAB or TECAB still has a limited role in myocardial revascularization, with a class II-b indication and a poor level of evidence.^[28] The only published prospective randomized trial (POLMIDES) evaluated 200 over a 12 months follow-up with no differences in mortality, myocardial infarction, repeated revascularization or other adverse events. However, the follow-up is still inadequate to reflect long-term effects, and participants continue to be monitored.^[29] Current literature evaluates mainly observational cohorts over a short term follow up. Potential benefits for minimally invasive HCR may be particularly important for higher risk patient. Minimally invasive surgical revascularization proved to be equally effective compared to standard surgical practice, and therefore the benefits arising from a less invasive approach can be translated into the HCR scenario. Regardless of the specific approach used, minimally invasive CABG is safe with an extremely low early mortality and freedom from reintervention, and effective with excellent survival and freedom from major adverse cardiac events.^[30] EACAB was found to be less traumatic than MIDCAB and less resource-intensive than TECAB, while EACAB carries an extremely low mortality rate (less than 1%) with a 5-year event-free survival above 90%.^[30] Robotically assisted procedures are the most resource-intensive, but were associated with excellent clinical outcomes in safety and efficacy in selected centers.^[30] A recent meta-analysis concluded that TECAB and RACAB are safe and feasible therapies for CAD, with reduced incidence of major adverse cardiac events after surgery. TECAB and RACAB were also shown not to increase graft stenosis rate and need for reintervention compared with standard CABG,^[31] and TECAB proved to reduce surgical trauma, decrease length of hospital stay and improve quality of life.^[32] Repossini, *et al.*,^[33] recently published their experience of 100 patients with multivessel CAD who underwent minimally invasive HCR with MIDCAB, summarizing their indications and suggesting that this strategy reduced the surgical trauma without reducing the quality of the results, thus representing the “best of both worlds” through a combination of long-term survival advantage of LIMA-to-LAD grafts and PCI with newer generation drug eluting stents to non-LAD vessels.^[34]

High risk patients may intuitively benefit most from this less invasive approach, but it also requires single-lung ventilation, which can be not well tolerated in patients with severe chronic lung disease, and in much overweight patients, the procedure may be technically challenging.^[27,35] Obese patients are generally excluded from the observa-

tional studies, due to the limited intra-thoracic space causing difficulties in managing surgical tools through minimally invasive chest openings. Intra-operative factors, such as intra-myocardial LAD artery, severely calcified LAD, pleural adhesions and inadequate stabilization of the heart may pose severe limitations to the surgical procedure. These minimally invasive techniques have been shown to be effective in improving recovery and reducing hospital stay, but are also generally burdened with concerns about the reduced surgical view, which might lead to technical difficulties in performing sutures by hand or in case of reoperation for bleeding. Other main concerns of this procedure include the expensive equipment associated with a steep learning curve for the surgeon, compared with more conventionally revascularization technique.^[32] Practice and training to minimally invasive CABG is extremely important and should be included in any residency program, as those procedures will become part of the routine skills for future surgeons. Risk of conversion from minimally invasive to standard surgical approach is three times greater for surgeons who performed less than 20 cases compared with more experienced colleagues, and learning curve is characterized by a progressively decreased operating time, conversion rate and short term mortality.^[32,36,37] Also, appropriate patients' selection is crucial to minimize the risk of intra-operative and postoperative complications. Results from clinical trials are heterogeneous and few studies report long-term outcomes.^[32] Generally, most of the studies with minimally invasive CABG included young patients with a low EuroSCORE, and those population does not adequately represent the geriatric cohort referred to the heart team.

HCR requires by itself a multidisciplinary team, and current studies in cardiology, pharmacology and cardiac surgery may rapidly accelerate the evolution of this practice. Each minimally invasive HCR with one-stage or two-stage approach with different sequence and intra-procedural delays, need to be compared with standard CABG, off-pump surgery or PCI, in order to delineate the most successful HCR strategy. Considering the importance of patients' selection for outcomes, eligibility for minimally invasive HCR should be carefully evaluated by the heart team, as outlined by Repossini, *et al.*^[33] Future clinical trials may help in defining the correct indications for HCR, which are currently based on single center experiences. The progressive introduction of SYNTAX score II, which provides information about both anatomical and clinical features of the patient,^[38,39] may help in identifying subsets of patients which would benefit more from HCR.^[40,41] Similarly, significance of coronary lesions is gradually being evaluated physiologically by means of fractional flow reserve or in-

stantaneous wave free ratio. Physiology-driven PCI proved to be more effective in the evaluation of coronary stenosis, and should be integrated in HCR protocols.^[42,43] As far as pharmacologic advances, cilostazol, a selective inhibitor of type-3 phosphodiesterase, has been considered as an integration to the common dual anti-platelet therapy, known as triple antiplatelet therapy (TAPT). TAPT was shown to reduce the incidence of major adverse cardiovascular events and target revascularization compared with traditional DAPT, without increasing bleeding. A recent meta-analysis of randomized trials concluded that cilostazol-based TAPT is associated with improved angiographic outcomes and decreased risk of repeated revascularization compared with DAPT. New antiplatelet agents or TAPT might improve clinical outcomes after HCR procedures, and these innovations should be taken into accounts in future clinical trials.^[14,44,45]

In conclusion, geriatric patients with CAD should be carefully evaluated by a dedicated heart team before being considered unsuitable or at extreme risk for revascularization. Such patients should not be labeled as untreatable without proper evaluation. Recent evidences seem to indicate that IMR should be avoided, and innovative strategies need to be developed to achieve CMR even in elderly patients. Off-pump CABG carries lower risks compared to the classic on-pump procedures, as circumvents the complications related to cardiopulmonary bypass and does not imply cardioplegic arrest, and LIMA-to-LAD revascularization using off-pump CABG is a safe and lasting solution. To this extent, newer minimally invasive solutions allow to achieve surgical LAD revascularization, and can be associated with percutaneous completion of revascularization to achieve minimally invasive HCR. In experienced hands, minimally invasive HCR may represent a very attractive technique and might provide optimal results especially in challenging patients, such as patients with advanced age or multiple comorbidities. A wider use of this technique, associated with adequate studies and clinical trials, might confirm if minimally invasive HCR is the most appropriate treatment among elderly patients.

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