

Angina after incomplete revascularization: therapeutic solutions

Enrico Natale, and Maria Denitza Tinti

UOC Cardiologia 1, Ospedale San Camillo, Roma

KEYWORDS: Complete coronary revascularization; Incomplete coronary revascularization; Angina; Ranolazine; Ivabradine

Angina in patients with stable coronary artery disease has a prevalence in the order of 58%, and influences quality of life as well as being associated with a yearly mortality rate between 1.2% and 2.4%.¹ The yearly rate of non-fatal myocardial infarction varies between 0.6% reported in the Second Randomized Intervention Treatment of Angina (RITA-2)² trial, and 2.7% in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE)³ trial. Besides less common conditions, such as micro-vascular pathology, hypertrophic cardiomyopathy or aortic valve disorders, stable angina is characteristically secondary to epicardial coronary arteries disease. Multi-vessels coronary artery disease (MVCAD), is conventionally define as a stenosis of >50% affecting more than one epicardial vessel, is diagnosed in 40-60% of the patients undergoing coronary angiogram and is associated with a worst prognosis than single vessel disease.⁴ Notwithstanding these data, both the extent of revascularization and the technique to achieve it, coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), are still unsettled. The goal of complete coronary revascularization (CR) has been explored for over 25 years in patients undergoing CABG. Coronary Artery Surgery Study (CASS) registry demonstrated that patients with MVCAD receiving three or more bypasses had a better survival than patients receiving only one or two.⁵ The CR concept has been successively extended to PCI. Nonetheless solid evidences, from randomized clinical trials (RCTs), proving the superiority of CR over incomplete revascularization (IR) are lacking. The available data derive from observational studies, subgroups analysis and *post hoc* of RCT and meta-analyses. The mode of revascularization (CABG vs. PCI) is not only dependent on the anatomical characteristics of the lesion [high SYNTAX (SYNergy between PCI with TAXUS and Cardiac Surgery) score, tortuosity, calcification, bifurcation lesions, and vessel diameter], but also relate to

the patients comorbidities (frailty, renal insufficiency, and diabetes).⁶ The occurrence of IR could then represent a marker of complexity, thus identifying high-risk patients. Accordingly the characteristics of patients enrolled in clinical trial represent an important confounding factor, shaping the data in favour of CR by selecting healthier patients when compared with the ones encountered in daily clinical practice. Furthermore, there is no general consensus as to the definition of CR. An adequate revascularization should be defined not only by the severity of the stenosis or the diameter of the vessel, but also in keeping with its ischaemic significance and the 'viability' of the myocardium served by the vessel. On the other hand 'anatomically complete revascularization' and 'functionally adequate revascularization' are not always synonyms, where the first refers to revascularization of all angiographically significant lesions, and the latter to revascularization of all lesions serving ischaemic but viable myocardium, or associated with a significantly ischaemic fractional flow reserve (FFR). The difference between anatomical and functional revascularization is particularly relevant when considering patients with documented myocardial necrosis, in whom the 'viable' myocardium should be served by coronary arteries with significant stenoses. According to the most common definition, anatomical CR is intended as the treatment of all coronary segments >1.5 mm in diameter and with ≥50% stenosis irrespective of the viability of the territory supplied; adequate functional revascularization, on the other hand, requires that the same lesions supply viable myocardium (myocardium-specific) or have <0.80 FFR (lesion-specific). IR occurs ever more frequently, reflecting a change in the patients population with chronic ischaemic cardiomyopathy, nowadays including older patients, with multiple comorbidities and with complex coronary lesions. Lacking dedicated clinical trials, the vast majority of the data are derived from registries and studies on CABG or

PCI, providing contrasting results with the *post hoc* analyses which, at times, are also of difficult interpretation, mostly because the absence of uniform definition of IR. Regardless the type of revascularization, IR significantly impact on prognosis and the occurrence of major adverse cardiovascular events, which appear to be related to the presence of inducible ischaemia and myocardial viability. Medical therapy directed at angina control and prevention of ischaemic events has a significant role. Recent anti-angina medications, ranolazine and ivabradine, are very useful for patients in whom control of angina and improved quality of life are important therapeutic goals, regardless the long term effects on prognosis. The choice of the type of revascularization, and its strategy, should follow a careful analysis of the patient, his/her clinical history and comorbidities.

Conflict of interest: none declared.

References

- Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot J-S, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabaté M, Senior R, Taggart DP, van der Wall EE, Vrints CJM, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Rydén L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease. *Eur Heart J* 2013;**34**:2949-3003.
- Henderson RA, Pocock SJ, Clayton TC, Knight R, Fox KA, Julian DG, Chamberlain DA. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. *J Am Coll Cardiol* 2003;**42**: 1161-1170.
- Shaw LJ, Berman DS, Maron DJ, Mancini GBJ, Hayes SW, Hartigan PM, Weintraub WS, O'Rourke RA, Dada M, Spertus JA, Chaitman BR, Friedman J, Slomka P, Heller GV, Germano G, Gosselin G, Berger P, Kostuk WJ, Schwartz RG, Knudtson M, Veledar E, Bates ER, McCallister B, Teo KK, Boden WE. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation* 2008;**117**:1283-1291.
- Zimarino M, Curzen N, Cicchitti V, De Caterina R. The adequacy of coronary revascularization in patients with multivessel coronary artery disease. *Int J Cardiol* 2013;**168**:1748-1757.
- Bell MR, Gersh BJ, Schaff HV, Holmes DR, Fisher LD, Alderman EL, Myers WO, Parsons LS, Reeder GS. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. *Circulation* 1992;**86**: 446-457.
- De Bruyne B. Multivessel disease: from reasonably incomplete to functionally complete revascularization. *Circulation* 2012;**125**:2557-2559.