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The everlasting dispute between coronary bypass and angioplasty in patients with multivessels coronary artery disease: results of the SYNTAX II study

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Coronary angioplasty, introduced 40 years ago, has seen significant technologic progress, particularly in the development of stents,[1] in the understanding of coronary physiology,[2–4] and coronary imaging, becoming the standard coronary revascularization technique for patients with non-complicated coronary artery disease. Nonetheless, in patients with three vessels coronary artery disease (3VD), the choice between percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG) still remains problematic. In the last few years, efforts have been made to identify objective parameters able to guide the therapeutic option in patients with multivessels disease. The SYNTAX I (SYNergy between PCI with TAXUS and Cardiac Surgery) study, published in 2013, compared PCI (with first generation stents) with CABG in patients with 3VD.[5] The 5 years results of the SYNTAX I documented that PCI had a higher mortality rate, myocardial infarction, and need for repeated revascularization than CABG. Accordingly, CABG has confirmed the treatment of choice for patients with complex multivessels disease, while PCI was recommended as an acceptable alternative treatment for patients with uncomplicated disease (SYNTAX score intermediate or low). The study results regarding complex multivessels disease have been challenged by recent technologic and procedural advancements of PCI. Furthermore, it has become clear that the decision as to the strategy of revascularization should have not been based on coronary anatomy only [SYNTAX SCORE I (SS I) $\geq$ 22], as recommended by the guidelines,[6] but needed to consider the specifics of the patient clinical situation.

- SYNTAX SCORE I
- Age
- Glomerular filtration rate (CrCl mL/m)
- LVEF (%)
- Unprotected Left Main
- Sex
- COPD
- PAD

Figure 1 SYNTAX II variables. In the SYNTAX II score have been included eight variables to accurately predict 4 years mortality in the individual patient. For instance, a man 60 years old, with SYNTAX SCORE I of 30, and unprotected left main disease, creatinine clearance of 60 mL/m, left ventricular ejection fraction of 50%, and chronic obstructive pulmonary disease, would have a SYNTAX II score of 41 points (predicted 4 years mortality = 16.3%) in case of coronary artery bypass grafting, but 33 points (predicted 4 years mortality = 8.7%) in case of percutaneous coronary intervention. The same patients, but without chronic obstructive pulmonary disease, would have the same predicted mortality after coronary artery bypass grafting or percutaneous coronary intervention.

These considerations gave impetus for the introduction of the SYNTAX II score (SS II) (*Figure 1*).[7]

SYNTAX II score was developed,[7] with the aim of improving clinical risk stratification, and facilitate the decision as

to which revascularization technique should be preferred. The SS II besides the anatomical variables, includes also those clinical factors known to affect prognosis, such as unprotected left main disease, female gender, chronic obstructive pulmonary disease, left ventricular ejection fraction, renal function, and peripheral arterial disease (*Figure 1*).

The study demonstrated that clinical outcomes with the SYNTAX II strategy were associated with improved clinical results compared with the PCI performed in similar patients from the original SYNTAX I trial, with a lower incidence of Major Adverse Cardiovascular Event (MACCE), as determined by a reduction of the individual endpoints: myocardial infarction, need for revascularization, stent thrombosis after 1 year of follow-up.[8]

The main results of this study can be summarized as:

- Clinical outcomes with the SYNTAX II strategy were associated with improved clinical results compared with the PCI performed in similar patients from the original SYNTAX I trial with a lower incidence of MACCE, as determined by a reduction of the individual endpoints: myocardial infarction, need for revascularization, stent thrombosis after 1 year of follow-up.
- Short-term results of patients at intermediate anatomical risk (SS I 23-32) treated with PCI according to the SS II, had similar results than patients at low anatomical risk (SS I $\leq$ 22).
- A physiologic evaluation was possible in 75% of the lesions, and contributed to delaying the treatment of 25% of the lesion studied.
- The systematic use of IVUS (IntraVascularUltraSound) guided stent implantation determined a further stent optimization (mostly post-dilatation) in 32.2% of the lesion treated.
- Contemporary chronic total occlusion revascularization techniques are associated with significantly improved results.

The SYNTAX II study is the demonstration that PCI practiced with the improved technologic and pharmacologic strategies available today provides a better prognosis than the procedure employed for the patients in the SYNTAX I study. Furthermore, the decision to proceed with CABG should not only be based on the coronary anatomy (SS I $\geq$ 22), but should include the clinical parameters included in the SYNTAX II score. Second generation stents, IVUS guidance, iFR/FFR, and a careful implantation technique, all contributed to the improvement of the clinical results of PCI. The long-term follow-up of the study will provide information regarding the persistence of the results in the long term, and whether it is safe to delay treatment of coronary lesions based on iFR/FFR assessment.

In patients with 3VD, the choice between PCI or CABG should be made after careful assessment of the risks and benefits according to an overall evaluation which includes the anatomical/functional coronary situation and the clinical characteristics of every single patient. The choice, in light of the current data, is becoming more straightforward.

Conflict of interest: none declared.

References

1. Indolfi C, De Rosa S, Colombo A. Bioresorbable vascular scaffolds—basic concepts and clinical outcome. *Nat Rev Cardiol* 2016;**13**:719–729.
2. Indolfi C, Mongiardo A, Spaccarotella C, Torella D, Caiazzo G, Polimeni A, Sorrentino S, Micieli M, Sabatino J, Curcio A, De Rosa S. The instantaneous wave-free ratio (iFR) for evaluation of non-culprit lesions in patients with acute coronary syndrome and multivessel disease. *Int J Cardiol* 2015;**178**:46–54.
3. Davies JE, Sen S, Dehbi HM, Al-Lamee R, Petraco R, Nijjer SS, Bhindi R, Lehman SJ, Walters D, Sapontis J, Janssens L, Vrints CJ, Khashaba A, Laine M, Van Belle E, Krackhardt F, Bojara W, Going O, Härle T, Indolfi C, Niccoli G, Ribichini F, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Erglis A, Vinhas H, Canas Silva P, Baptista SB, Alghamdi A, Hellig F, Koo BK, Nam CW, Shin ES, Doh JH, Brugaletta S, Alegria-Barrero E, Meuwissen M, Piek JJ, van Royen N, Sezer M, Di Mario C, Gerber RT, Malik IS, Sharp ASP, Talwar S, Tang K, Samady H, Altman J, Seto AH, Singh J, Jeremias A, Matsuo H, Kharbanda RK, Patel MR, Serruys P, Escaned J. Use of the instantaneous wave-free ratio or fractional flow reserve in PCI. *N Engl J Med* 2017;**376**:1824–1834.
4. De Rosa S, Polimeni A, Petraco R, Davies JE, Indolfi C. Diagnostic performance of the instantaneous wave-free ratio: comparison with fractional flow reserve. *Circ Cardiovasc Interv* 2018;**11**:e004613.
5. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Ståhle E, Colombo A, Mack MJ, Holmes DR, Morel MA, Van Dyck N, Houle VM, Dawkins KD, Serruys PW. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 2013;**381**:629–638.
6. Authors/Task Force Members, Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014;**35**:2541–2619.
7. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR, Mack M, Feldman T, Morice M-C, Ståhle E, Onuma Y, Morel M-A, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet* 2013;**381**:639–650.
8. Escaned J, Collet C, Ryan N, Luigi De Maria G, Walsh S, Sabate M, Davies J, Lesiak M, Moreno R, Cruz-Gonzalez I, Hoole SP, Ej West N, Piek JJ, Zaman A, Fath-Ordoubadi F, Stables RH, Appleby C, van Mieghem N, van Geuns RJ, Uren N, Zueco J, Buszman P, Iñiguez A, Goicolea J, Hildick-Smith D, Ochala A, Dudek D, Hanratty C, Cavalcante R, Kappetein AP, Taggart DP, van Es G-A, Morel M-A, de Vries T, Onuma Y, Farooq V, Serruys PW, Banning AP. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur Heart J* 2017;**38**:3124–3134.