



Debate. Revascularization of nonculprit lesions in ACS: physiology or OCT-guided or both? Perspective from imaging



A debate. Revascularización de lesiones no culpables en SCA. ¿Guiada por fisiología, por OCT o por ambas? Perspectiva desde la imagen

Josep Gómez-Lara*

Servicio de Cardiología, Hospital Universitari de Bellvitge, Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), Universitat de Barcelona, L'Hospitalet de Llobregat, Barcelona, Spain

SEE RELATED CONTENT:
<https://doi.org/10.24875/RECICE.M22000359>

QUESTION: What is the benefit of intravascular imaging modalities—specifically the optical coherence tomography (OCT)—in the context of nonculprit lesions of an acute coronary syndrome (ACS)?

ANSWER: The publications of the COMPLETE and FLOWER MI clinical trials has changed the management of nonculprit lesions tremendously in patients with ACS jeopardizing the role of the pressure guidewire guiding the revascularization of these lesions.^{1,2} In the COMPLETE trial, angiography-guided complete revascularization reduced the rates of death and infarction compared to the optimal medical therapy (OMT).¹ We should mention that over 80% of the lesions included had an angiographic percent diameter stenosis $\geq 70\%$.¹ In the FLOWER MI trial that included less severe nonculprit lesions, pressure guidewire-guided complete revascularization reduced the number of lesions treated (45% fewer lesions) compared to angiography-guided complete revascularization with a similar rate of events in both strategies.² However, a subanalysis of the group of patients treated with pressure guidewire guidance revealed that patients with fractional flow reserve (FFR) values ≤ 0.80 (stented according to protocol) had fewer events compared to patients with FFR values > 0.80 (treated with OMT).³ This has aroused controversy regarding the utility of the pressure guidewire in this context. Probably the reason why the FFR has such a low negative predictive value is the lack of information on the composition of the plaque of the target lesion. In a subanalysis of the COMPLETE trial where nonculprit lesions were treated with OCT, it was reported that $> 35\%$ of the lesions with stenosis $\geq 70\%$ were classified as vulnerable plaques compared to 25% of intermediate lesions (stenosis between 50% and 69%).⁴

Vulnerable plaques include a high lipidic content and are covered by a thin fibrous layer ($\leq 65 \mu\text{m}$ according to pathological anatomy, which corresponds to $\leq 80 \mu\text{m}$ according to OCT if the axial resolution of this technique is taken into consideration).⁵ According to

the PROSPECT clinical trials, the use of intracoronary ultrasound and infrared spectroscopy can detect vulnerable plaques in nonculprit coronary arteries in patients with ACS, and the former are associated with a high risk of triggering ACS at 4-year follow-up (up to 18% if they had a minimum lumen area and a large plaque burden).^{6,7}

The role of OCT to detect vulnerable plaques in nonculprit lesions of ACS is still to be elucidated. However, since this intravascular imaging modality provides the highest resolution of all, it is probably the best imaging modality to assess the morphological characteristics of these lesions, particularly if they show signs of vulnerability.

Q.: How would you introduce the OCT in the assessment protocol of these lesion in relation to the pressure guidewire?

A.: In my opinion, the use of diagnostic intracoronary imaging modalities (whether with guidewire pressure or intravascular images) in severe nonculprit lesions (with percent diameter stenosis $\geq 70\%$) is not currently justified. Like I said before, severe nonculprit lesions on the angiography have high chances of being vulnerable plaques and, if untreated, are associated with a larger number of adverse events.^{1,4} As a matter of fact, with a level of evidence IA, the recent clinical practice guidelines from the American College of Cardiology and the American Heart Association published following the COMPLETE and FLOWER-MI trials recommend the revascularization of nonculprit lesions of ST-segment elevation ACS (STEACS) with percent diameter stenosis $\geq 70\%$ on the angiography.⁸

However, the role these diagnostic intracoronary imaging modalities play in intermediate lesions (stenosis between 40% and 69%) or even in angiographic segments without overt angiographic lesion is still to be elucidated. An early assessment of intermediate

* Corresponding author.

E-mail address: gomezjosep@hotmail.com [J. Gómez-Lara].

[@josep98564779](https://twitter.com/josep98564779)

Online 13 March 2023.

2604-7322 / © 2023 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

lesions with FFR through pressure guidewire allows us to select those lesions that, *per se*, trigger ischemia. According to former studies on this type of intermediate lesions, nearly 45% of them show FFR values ≤ 0.80 and, therefore, have an indication for revascularization.^{2,9} As a matter of fact, the positive predictive value of FFR values ≤ 0.80 is not discussed here, and the management of lesions with pathological FFR values is currently backed by the routine clinical practice guidelines with a level of evidence IA.^{8,10} In my opinion, the utility of the OCT should be reviewed in lesions that don't trigger ischemia (like lesions with FFR values > 0.80) and when the management of nonculprit lesions is purely preventive.

Up until now, only 1 study has assessed the preventive treatment of nonculprit lesions with characteristics of vulnerability. The PROSPECT-ABSORB trial randomized nonculprit lesions with characteristics of vulnerability on the intravascular echocardiography to receive bioresorbable stents or OMT. In this trial, the preventive treatment of vulnerable plaques reduced the rates of events compared to treatment although the study was not designed to compare clinical events.¹¹

Q.: In your opinion, what will the future bring, new protocols combined? maybe new techniques?

A.: The risk associated with a vulnerable plaque in patients with multivessel ACS is currently under study and discussion. After an infarction, over 50% of the ischemic events described at follow-up are due to nonculprit lesions.⁷ The Spanish Society of Cardiology Working Group on Intracoronary Diagnosis of the Interventional Cardiology Association has inspired a randomized clinical trial that will include over 40 Spanish centers. The VULNERABLE trial (NCT 05599061) will study nearly 2500 patients with STEACS and angiographically intermediate nonculprit lesions (angiographic percent diameter stenosis between 40% and 69%). Per protocol, these lesions will be studied in an elective procedure different from the index procedure with which the culprit lesion was treated successfully. All eligible lesions will be interrogated using the pressure guidewire, and those with pathological FFR values (≤ 0.80) will be stented and considered a selection failure (it is estimated that nearly 40% of the lesions studied). The remaining lesions (1500 approximately) with FFR values > 0.80 will be studied with the OCT looking for characteristics of vulnerability. Lesions without these characteristics (an estimate of 900 lesions) will be treated with OMT and periodically followed to assess adverse events (within the VULNERABLE Registry). Finally, the study will include a total of 600 lesions with negative FFR but with characteristics vulnerability on the OCT that will be randomized (1:1) to stenting or OMT (within the VULNERABLE clinical trial). The follow-up period scheduled for both registry patients and the clinical trial is 4 years. This is the first trial ever conducted with statistical power to assess the clinical effectiveness of preventive stenting of nonculprit lesions with characteristics of vulnerability according to the OCT.

Q.: How would you bring together the concepts of vulnerable plaque and vulnerable patient?

A.: In my opinion, patients with ACS have 3 different problems occurring simultaneously. First, like I mentioned before, they have a type of aggressive atherosclerosis with significant plaque burden and characteristics of vulnerability.⁴ Second, patients with ACS have a higher degree of microvascular dysfunction, not only in the infarct-related artery but also in other nonculprit arteries.¹² Pancoronary microvascular dysfunction is probably associated with a higher sensitivity to the chronic ischemia due to epicardial obstructive coronary lesions and the inability to create collateral circulation in the presence of a new acute complete obstruction (therefore associated with a higher risk of infarction). And third, patients with

ACS have elevated inflammatory markers, more platelet reactivity, and more thrombogenicity compared to chronic patients.¹³ As a matter of fact, anti-inflammatory treatments have proven capable of reducing adverse events in patients with ACS.¹⁴

Therefore, patients with ACS have anatomical, functional, and systemic inflammatory-thrombotic characteristics that clearly separate them from chronic patients. This differentiation is mainly based on a higher risk of new thrombotic events in the future. Some, actually, call them «vulnerable patients». The management of these «vulnerable» patients should address these 3 problems at the same time. Therefore, therapeutic advances are necessary to reduce the plaque burden and stabilize vulnerable plaques. Also, antiplatelet therapies to reduce ischemic risk, at least, until most vulnerable plaques have stabilized, and eventually therapies to reduce systemic inflammation and, probably, improve the endothelial function of these patients.

The role of preventive angioplasty with stenting in vulnerable plaques is still to be elucidated. Undoubtedly, one of the dilemmas we'll have to elucidate in the future is whether to choose intensive medical therapy with new drugs capable of stabilizing vulnerable plaques or «stabilization sealing» of neointimal tissue layer induced by stenting plus OMT.

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med.* 2019;381:1411-1421.
2. Puymirat E, Cayla G, Simon T, et al. Multivessel PCI Guided by FFR or Angiography for Myocardial Infarction. *N Engl J Med.* 2021;385:297-308.
3. Denormandie P, Simon T, Cayla G, et al. Compared Outcomes of ST-Elevation Myocardial Infarction Patients with Multivessel Disease Treated with Primary Percutaneous Coronary Intervention and Preserved Fractional Flow Reserve of Non-Culprit Lesions Treated Conservatively and of Those with Low Fractional Flow Reserve Managed Invasively: Insights from the FLOWER MI trial. *Circ Cardiovasc Interv.* 2021;14:e011314.
4. Pinilla-Echeverri N, Mehta SR, Wang J, et al. Nonculprit Lesion Plaque Morphology in Patients With ST-Segment-Elevation Myocardial Infarction: Results From the COMPLETE Trial Optical Coherence Tomography Substudies. *Circ Cardiovasc Interv.* 2020;13:e008768.
5. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol.* 2006;47:C13-18.
6. Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med.* 2011;364:226-235.
7. Erlinge D, Maehara A, Ben-Yehuda O, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study. *Lancet.* 2021;397:985-995.
8. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2022;145:e4-e17.
9. Koo BK, Kang J, Wang J. Fractional Flow Reserve or Intravascular Ultrasound for PCI. Reply. *N Engl J Med.* 2022;387:2099.
10. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2019;40:87-165.

11. Stone GW, Maehara A, Ali ZA, et al. Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque. *J Am Coll Cardiol.* 2020;76:2289-2301.
12. van de Hoef TP, Bax M, Meuwissen M, et al. Impact of coronary microvascular function on long-term cardiac mortality in patients with acute ST-segment-elevation myocardial infarction. *Circ Cardiovasc Interv.* 2013;6:207-215.
13. Matsuo K, Ueda Y, Nishio M, et al. Thrombogenic potential of whole blood is higher in patients with acute coronary syndrome than in patients with stable coronary diseases. *Thromb Res.* 2011;128:268-273.
14. Tardif JC, Kouz S, Waters DD, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. *N Engl J Med.* 2019;381:2497-2505.