Rev Port Cardiol. 2016;35(12):655–657

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Management of non-ST-elevation myocardial infarction: A constant challenge☆

Tratamento do enfarte do miocárdio sem elevação de ST: um eterno desafio...

Henrique Cyrne Carvalho[a,b]

[a] *Serviço de Cardiologia do Centro Hospitalar e Universitário do Porto, Hospital de Santo António, Porto, Portugal*
[b] *Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal*

Available online 1 December 2016

Growing recognition of the heterogeneity of clinical conditions associated with non-ST-elevation myocardial infarction (NSTEMI) has led to intense research on this entity in a search for the best therapeutic options.

NSTEMI is associated with higher rates of morbidity and mortality than other acute coronary syndromes (ACS)[1] and thus warrants thorough study.

The article by Gonzales-Cambeiro et al.[2] published in this issue of the *Journal* on the mortality benefit of long-term angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEIs/ARBs) after successful percutaneous coronary intervention (PCI) in NSTEMI gives this question a new impulse.

The authors of this observational study showed that in NSTEMI patients successfully treated by PCI, the use of ACEIs/ARBs was associated with a lower risk of four-year mortality. However, the high rate of multivessel disease, lack of information on the proportion of patients who underwent complete revascularization and on how soon PCI was performed, and the fact that the population was not stratified according to clinical severity by criteria such as the GRACE score, highlight certain variables that require particular attention in the assessment and treatment of this heterogeneous patient group.

The benefit of ACEIs/ARBs as an adjuvant therapy for ST-elevation myocardial infarction (STEMI) has long been known,[3–6] but conclusive evidence of their value in NSTEMI is lacking. The article by Gonzales-Cambeiro et al.[2] appears to demonstrate a reduction in all-cause mortality with ACEI/ARB use in this subgroup of ACS patients. But was it the drug treatment alone that was responsible for this benefit? In our opinion there are three factors that could have biased these results: (1) the timing of PCI; (2) the completeness of revascularization; and (3) the duration of antiplatelet therapy.

Let us now examine these three factors in detail.

(1) Analysis of the timing for invasive assessment of patients with non-ST-elevation ACS shows that the best strategy is always to perform it as soon as possible,[7,8] although in certain subgroups this is even more important, as timing can have significant effects on medium- and long-term outcome.[9] Earlier intervention is associated with lower mortality. Patients with higher clinical risk scores are known to benefit more from an earlier approach,[7–9] but it is these patients who frequently have to wait longer before intervention, since their circumstances are often less favorable in terms of the safety and efficacy of invasive procedures. Among such factors are female gender, advanced age, renal dysfunction and anemia. It can be a temptation not to treat these patients, because they

DOI of original article: http://dx.doi.org/10.1016/j.repce.2016.07.004
☆ Please cite this article as: Cyrne Carvalho H. Tratamento do enfarte do miocárdio sem elevação de ST: um eterno desafio.... Rev Port Cardiol. 2016;35:655–657.
E-mail address: henriquecyrnecarvalho@hotmail.com

are ''too sick'' or because the risk of intervention is too high.

Consequently, many of the results obtained in groups of consecutive patients do not accurately reflect the effect on the timing of intervention of the combined effect of these different factors, however clearly each of the individual variables involved has been identified and described.

Subgroup analysis according to risk scores and timing of intervention could help to determine the influence of different therapeutic strategies (pharmacological or otherwise) on clinical outcome and prognosis.

(2) The second factor relates to the proportion of patients with multivessel disease who did not undergo complete revascularization, which the article states was almost half of both study groups.

The importance of complete revascularization (immediate or staged) in reducing the need for repeat revascularization is accepted in STEMI patients, but there is no solid evidence that this also applies to mortality and reinfarction.[10,11] Its impact on mortality as a single endpoint is unknown, although it has been included in combined endpoints.[12,13]

The available evidence also supports complete revascularization in NSTEMI,[14] and recent studies recommend that revascularization be performed in a single procedure, since a staged approach is associated with a higher rate of major adverse cardiovascular and cerebrovascular events.[15]

The study by Gonzales-Cambeiro et al.[2] does not specify the number of patients who underwent complete revascularization, and this may have biased the results. Patients who would benefit most from complete revascularization are often those in whom it is more difficult to perform, because of three-vessel disease, diffuse disease, left main disease, left ventricular dysfunction, and similar conditions.

Thus, as in the question of the timing of intervention, the greatest difficulty in deciding the most appropriate approach in accordance with the state of the art comes when dealing with the most complex types of patient.

(3) Thirdly, it is important to discuss antiplatelet therapy, which is of great importance in patients with NSTEMI undergoing PCI.

We know that most patients in Gonzales-Cambeiro et al.'s study[2] were under dual antiplatelet therapy with aspirin and clopidogrel at hospital discharge, but they do not state what proportion continued this therapy for the full 12 months stipulated, how many discontinued it before, or how many continued it afterwards. The first two cases can affect outcome, while recent data[16] indicate that the third could have a positive impact on prognosis in selected patients with high ischemic risk and low bleeding risk.

Finally, another factor can have a significant impact on prognosis: left ventricular function. Most of the population in Gonzales-Cambeiro et al.'s study[2] had preserved (>50%) mean left ventricular ejection fraction (LVEF), with only a small proportion having LVEF $\leq$40% (less than 10% after propensity score matching). It thus appears that the mortality rates observed (around 16% in the untreated groups and almost 12% in the treated group), lower than the 22% predicted,[1] may be related to the proportion with preserved LVEF.

Despite this, ACEIs/ARBs would be expected to be less effective in patients with preserved LVEF. However, we are not told the percentage of patients who suffered reinfarction or target lesion failure during follow-up, and it is thus impossible to know how the above factors might have affected the results.

There is still considerable uncertainty concerning the treatment of NSTEMI, due mainly to the heterogeneity of its presentation and clinical course. Its poor prognosis means that improvements in treatment are particularly important. By three years after the index event, around 22% of NSTEMI patients have died.[1] This figure gives us pause for thought.

Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Fox KA, Carruthers KF, Dunbar DR, et al. Underestimated and under-recognized: the late consequences of acute coronary syndrome (GRACE UK-Belgian Study). Eur Heart J. 2010;31:2755–64.
2. Gonzales-Cambeiro MC, López-López A, Abu-Assi E, et al. Mortality benefit of long-term angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker after successful percutaneous coronary intervention in non-ST elevation myocardial infarction. Rev Port Cardiol. 2016;35:645–53.
3. Pfeffer MA, Lamas GA, Vaughan DE, et al. Effect of captopril on progressive ventricular dilatation after anterior myocardial infarction. N Engl J Med. 1988:319–80.
4. Sharpe N, Smith H, Murphy J, et al. Early prevention of left ventricular dysfunction after myocardial infarction with angiotensin-converting-enzyme inhibition. Lancet. 1991;337:872.
5. St John Sutton M, Pfeffer MA, Plappert T, et al. Quantitative two-dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after acute myocardial infarction. The protective effects of captopril. Circulation. 1994;89:68.
6. Hall AS, Murray GD, Ball SG. Follow-up study of patients randomly allocated ramipril or placebo for heart failure after acute myocardial infarction: AIRE Extension (AIREX) Study. Acute Infarction Ramipril Efficacy. Lancet. 1997; 349:1493.
7. Katritsis DG, Siontis GCM, Kastrati A, et al. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. Eur Heart J. 2011;32:32–40.
8. Puymirat E, Taldir G, Aissaoui N, et al. Use of invasive strategy in non-ST-segment elevation myocardial infarction is a major determinant of improved long-term survival: FAST-MI (French Registry of Acute Coronary Syndrome). JACC Cardiovasc Interv. 2012;5:893–902.
9. De Winter RJ, Tijssen JGP. Non-ST-elevation myocardial infarction: revascularization for everyone? JACC Cardiovasc Interv. 2012;5:903–5.
10. Amartya K, et al. Complete revascularization for multivessel disease ST elevation myocardial infarction: insights from an updated meta-analysis. Circulation. 2015:10132.

11. Bangalor S, Toklu B, Wetterslev J. Complete versus culprit-only revascularization for ST-segment-elevation myocardial infarction and multivessel disease. A meta-analysis and trial sequential analysis of randomized trials. Circ Cardiovasc Interv. 2015;8:e002142.
12. Sekercioglu N, Spencer FA, Lopes LC, et al. Culprit vessel only vs immediate complete revascularization in patients with acute ST-segment elevation myocardial infarction: systematic review and meta-analysis. Clin Cardiol. 2014;37:765–72.
13. Gershlick A, Khan JMNK, Damian JK, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease. J Am Coll Cardiol. 2015;65: 963–72.
14. Dimitrov N, Karamfilov K, Simova II, et al. Complete versus target-vessel revascularization in NSTEMI patients. J Am Coll Cardiol. 2015;65(17_S):S7–8, http://dx.doi.org/10.1016/j.jacc.2015.03.061.
15. Sardella G, Lucisamo L, Garbo R, et al. Single-staged compared with multi-staged PCI in multivessel NSTEMI patients: the SMILE Trial. J Am Coll Cardiol. 2016;67:264–72.
16. Bonaca MP, Deepak LB, Cohen M, et al. Long-term use of ticagrelor in patients with prior myocardial infarction. PEGASUS-TIMI 54. N Engl J Med. 2015;372:1791–800.