



## EDITORIAL COMMENT

# Multivessel revascularization in non-ST-elevation acute coronary syndrome: Should it become the rule in all patients? ☆



## Revascularização multivaso na síndrome coronária aguda sem supradesnivelamento do segmento st: deve ser a regra em todos os doentes?

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An invasive strategy is increasingly used in patients with non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS), especially when the risk of events is intermediate or high.<sup>1,2</sup> In confirmed obstructive coronary artery disease, coronary revascularization reduces both mortality and non-fatal events.<sup>1</sup> Around 50% of patients with NSTEMI-ACS have multivessel disease, and so the type and form of revascularization may require an individualized decision-making process, including discussion in the heart team.<sup>1,3</sup> One of the issues facing the care team is whether revascularization of patients with NSTEMI-ACS and multivessel disease should be incomplete (only the culprit artery) or complete, and in the latter case, whether it should be carried out during the same procedure or in subsequent procedures. There is growing evidence that multivessel revascularization, including of non-culprit lesions, in patients with ST-segment elevation myocardial infarction is safe and reduces the risk of recurrent events.<sup>4–6</sup> Although it is tempting to extrapolate these results to the NSTEMI-ACS patient population, it is important to note that there have been no prospective randomized tri-

als that confirm the superiority and safety of a multivessel revascularization strategy in the latter group. Furthermore, in patients with myocardial infarction presenting in cardiogenic shock, revascularization of the culprit artery only may be superior to multivessel revascularization, as recently demonstrated in a randomized trial.<sup>7</sup>

In this issue of the *Journal*, Correia et al.<sup>8</sup> compare a multivessel revascularization strategy with culprit-only revascularization in a population of patients with NSTEMI-ACS and multivessel disease. This observational, retrospective and longitudinal study included all patients with ACS who underwent percutaneous coronary intervention at a single hospital between 2010 and 2013. Among NSTEMI-ACS patients, the proportion with multivessel disease was 46%, defined as the presence of at least two lesions deemed angiographically significant ( $\geq 50\%$  stenosis) in different coronary artery territories. The population analyzed consisted of 202 patients, 71 (35%) of whom underwent multivessel revascularization, while 131 (65%) underwent culprit-only revascularization. The culprit artery was identified using a combination of clinical, electrocardiographic, echocardiographic and angiographic data, and the decision to perform coronary revascularization of non-culprit arteries and the timing of the procedure were determined by the interventional cardiologist and clinical cardiologist, or by the heart team, as appropriate. Multivessel revascularization was defined as intervention (percutaneous or surgical) on two or more lesions in different coronary artery territories, during the

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initial procedure (first stage) or planned in the following 30 days (second stage). The minimum follow-up was three years, with a median of 1520 days (4.1 years), and the analysis included occurrence of death, reinfarction, unplanned revascularization and major adverse cardiovascular events (mortality, reinfarction, stroke or heart failure). To minimize the bias created by factors influencing the selection of revascularization type, a survival analysis was performed on a population divided by propensity score matching, which included 66 patients in each group.

It is important to note that the NSTEMI-ACS patients analyzed by Correia et al.<sup>8</sup> constituted a selected population, since they only included those with confirmed multivessel disease for whom it was decided to adopt an invasive strategy by percutaneous intervention. Nevertheless, their demographic and clinical characteristics are consistent with those reported in real-world registries.<sup>2</sup> Additionally, there were no significant differences between groups with different revascularization strategies, either before or after propensity score matching.

In patients who underwent multivessel revascularization, most (66%) were treated in a single procedure, but only 52% underwent complete revascularization. In those in whom only the culprit artery was treated, 35% did not have their other stenoses treated because these were considered insignificant (<70%), 18% because they had diffuse or complex disease, 8% because they had chronic occlusions, and for more than one reason in the remainder.

There were no significant differences between the groups with regard to clinical events during hospital stay. However, in medium- to long-term follow-up, patients who underwent multivessel revascularization had a lower incidence of reinfarction (5.6% vs. 16.8%) and unplanned revascularization (5.6% vs. 15.3%), with no differences in mortality, stroke or heart failure. Patients who underwent culprit-only revascularization thus had around twice as many events in long-term follow-up of the composite endpoint of death, reinfarction or unplanned revascularization. The results before and after propensity score matching were similar. A meta-analysis by Jang et al., which analyzed eight observational studies comparing multivessel with culprit-only revascularization, showed that the former strategy reduces the rate of unplanned revascularization by 25% and is associated with a non-significant reduction of approximately 15% in reinfarction and death.<sup>9</sup>

If multivessel revascularization is to become the rule in patients with NSTEMI-ACS, it is important to discuss its timing. In the study by Correia et al.,<sup>8</sup> around a third of patients who underwent multivessel revascularization did so in a second procedure up to 30 days after the acute event. This staged strategy is questionable, since in the SMILE trial, single-stage multivessel revascularization reduced the risk of recurrent events by almost 50% compared with deferred multivessel revascularization (second procedure performed three to seven days after the first).<sup>10</sup> This reduction was mainly due to a significant reduction in the rate of unplanned revascularization. However, it is important to note that a trend toward less mortality and reinfarction was also found in patients who underwent single-stage revascularization, with no increase in complications such as contrast-induced nephropathy or periprocedural infarction.<sup>10</sup>

Another factor to consider when deciding on the type of revascularization is coronary anatomy and disease extent. In the study by Correia et al.,<sup>8</sup> over a quarter of the patients did not undergo multivessel revascularization because they had complex disease and/or chronic occlusions. The authors do not report the SYNTAX score or any other marker of the severity and extent of coronary artery disease, so the decision to revascularize only the culprit artery may have been due to the patient's anatomical characteristics.<sup>1</sup> More complex coronary artery disease is known to be associated with a higher rate of recurrent events in patients with NSTEMI-ACS. It is therefore important to consider which strategy will enable the most complete revascularization in an individual patient with complex lesions.<sup>1,11</sup> Similarly, intermediate lesions should also be assessed thoroughly. In Correia et al.'s study, in 35% of patients only the culprit artery was revascularized because the other lesions were defined as moderate, i.e. with <70% stenosis. In this group, functional assessment of the lesions could have modified the revascularization strategy.<sup>12</sup> In a sub-analysis of the FAME study, which included 328 patients with NSTEMI-ACS, the decision to revascularize on the basis of fractional flow reserve was associated with a 19% relative reduction and a 5% absolute reduction in the risk of events (including death from any cause, infarction, and any repeat revascularization).<sup>13</sup> The value of using functional assessment to guide the revascularization strategy has also been validated in another study, which included a sample of Portuguese NSTEMI-ACS patients.<sup>14</sup>

The decision to revascularize only the culprit artery should also take into account the difficulty in identifying this artery, which may be an additional challenge in selecting the strategy.<sup>13</sup> In the study by Correia et al.,<sup>8</sup> the culprit artery was determined without the use of a predefined protocol and in a somewhat subjective manner. However, in around half of patients with NSTEMI-ACS, there may be multiple complex plaques responsible for the infarction, and identification of the culprit artery may not be straightforward.<sup>15,16</sup> Additionally, incomplete revascularization is associated with increased risk of events, especially in patients with NSTEMI-ACS, as demonstrated in various studies.<sup>1,16</sup> These facts further support the role of a multivessel revascularization strategy in NSTEMI-ACS.

In conclusion, the study by Correia et al.<sup>8</sup> supports the idea that multivessel revascularization should be the rule in patients with NSTEMI-ACS, since it is a proven and safe strategy that can have a significant impact on reducing the risk of events in the medium to long term.

## Conflicts of interest

The author has no conflicts of interest to declare.

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