CULPRIT-SHOCK study

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SUMMARY

The treatment of patients with ST-segment elevation myocardial infarction concomitant with the presence of multivessel disease has been studied in several recent studies with the purpose of defining the need, as well as the best moment to approach residual lesions. However, such studies included only stable patients. The best therapeutic approach to cardiogenic shock secondary to acute coronary syndrome, however, remains controversial, but there are recommendations from specialists for revascularization that include non-event related injuries. Recently published, the CULPRIT-SHOCK study showed benefit of the initial approach only of the injury blamed for the acute event, in view of the multivessel percutaneous intervention, in the context of cardiogenic shock. In this perspective, the authors discuss the work in question, regarding methodological questions, limitations and clinical applicability.

KEYWORDS: *Myocardial infarction. Cardiogenic shock. Percutaneous coronary intervention.*

In acute coronary syndromes with ST segment elevation (STEMI), primary angioplasty of the culprit artery is the therapy of choice, and should be performed as fast as possible in individuals who present themselves in a timely manner for this, according to national and international guidelines. Approximately 65% of the coronary angiography performed in this context, however, present multivessel disease, with significant lesions affecting territories not related to the acute event.[1] Until recently, the main international guidelines (American College of Cardiology Foundation/2013 American Heart Association and 2012 European Society of Cardiology)[2,3] recommended that residual lesions should not be treated concomitantly with the treatment of culprit lesions, based mainly on subgroup analyses and retrospective records.[4,5]

However, four randomized trials were designed to evaluate the possible benefit of early approach of non-infarction-related lesions, whether in the same procedure as primary angioplasty or at some point prior to hospital discharge.[6-9] Although there were methodological differences in the method for evaluation of angiographic severity (anatomical: PRAMI> 50% and CVLPRIT> 70%, or functional guided by FFR: DANAMI-3 PRIMULTI and COMPARE)

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and at the moment of approaching the residual lesions (intervention in the initial angiography: COMPARE-ACUTE and PRAMI; in a second procedure still during hospitalization: DANAMI-3 PRIMULTI; or at any time before discharge, either during the initial catheterization or after it: CVLPRIT), when evaluating data from all studies together, the option for early multivessel revascularization resulted in reduction of cardiovascular adverse events at the expense of lower incidences of additional revascularization and mortality of cardiac etiology.[10]

Thus, the latest guideline of the 2017 European Society of Cardiology recommends routine revascularization of non-culprit lesions in STEMI before hospital discharge (IIa recommendation class, level of evidence A).[11] However, in the mentioned studies, patients in cardiogenic shock were not included in the analyses, leaving a gap of evidence in this scenario.

Approximately 5%-10% of STEMI evolve with cardiogenic shock and, consequently, a high in-hospital mortality rate (around 50%)[12,13]. The majority of cases involve multivessel disease in association with the coronary lesion responsible for the acute event.[14] However, there is still doubt about the best form of therapeutic approach in this scenario.

Published in 1999, in a sample with 302 patients, the SHOCK trial evaluated the best therapeutic approach in cardiogenic shock secondary to STEMI: early revascularization (surgical or percutaneous) or initial drug therapy. Although there was no difference between groups in the primary outcome of mortality at 30 days, there was superiority of early interventionist behaviour, with a reduction in mortality at six months. In clinical practice, before a patient with cardiogenic shock, considering this study, we should prioritize myocardial revascularization.[15]

Being well-defined the option for the intervention strategy in patients who developed with cardiogenic shock in the acute context, we lacked good evidence in the comparison of the different approaches of multivessel disease in the context of cardiogenic shock: revascularization only of the culprit artery or complete multivessel revascularization.

The CULPRIT-SHOCK study was then designed to test the hypothesis that angioplasty only of the culprit lesion, with the option of staged revascularization of the residual lesions at a second moment (considering functional evaluation for FFR, symptoms and neurological status), would have better outcomes than the immediate treatment of all major stenosis (over 70% by anatomical evaluation, including chronic occlusions), in the acute phase of cardiogenic SHOCK associated with multivessel coronary disease.[16]

In a sample with 706 subjects, a primary outcome comprised of all-cause death or renal insufficiency requiring 30-day renal replacement therapy was considered. Populations of the two groups were similar, and mostly composed of tri-arterial patients (63%), with involvement of the anterior descending artery (around 40%) and presenting ST elevation on admission (about 62%). Approximately 22% of patients had at least one chronic coronary occlusion in both arms.

About 80% of the individuals in the multivessel revascularization group underwent complete immediate revascularization, while in the intervention group only in the culprit lesion, only 7.6%. In the latter group, 17.7% of the patients were submitted to angioplasty staged from non-infarct-related lesions.

Regarding the primary outcome, the group approaching only the culprit lesion presented a lower incidence of events in 30 days [45.9% x 55.4%; relative risk (RR), 0.83; 95% CI, 0.71-0.96; p = 0.01], at the cost of lower mortality (43.3% x 51.6%, RR 0.84, 95% CI, 0.72-0.98, p = 0.03). In addition, the amount of contrast used and the fluoroscopy time were also significantly lower in this group. Considering the rates of renal replacement therapy, there was no significant difference between the groups, as well as in the analysis of the secondary outcomes.

The physiopathological explanations of the results of this study, as the editorial itself warns, are still speculative.[17] It is difficult to expect an increase in mortality in a therapeutic group with higher rates of complete revascularization. The question, however, focuses on the timing of this more complete approach. The recommendation of a multivessel approach in the period of hemodynamic instability may have contributed to the increase in procedure time, greater contrast volume used and potential complications related to angioplasty, which may lead to volume overload and increased inflammatory activity, with negative repercussions myocardial recovery. The approach guided only by visual estimation of residual lesions (without documentation of FFR ischemia) and the approach of chronic occlusions may also have contributed to this outcome.

In addition, the increase in platelet reactivity associated with a prothrombotic effect due to the

cardiogenic shock state may increase the risk of ischemia and infarction during intervention in the residual arteries and, consequently, deteriorate left ventricular function.

It is worth noting that this study is not free of limitations. The management of cardiogenic shock is complex and multifactorial, allowing the appearance of biases and occasional findings in the analyses. In spite of the difference in mortality observed between the strategies, the high mortality rates similar to those observed in the Shock study 18 years ago (46.7% versus 56% for the conservative treatment and intervention groups, respectively) were observed. There was also a considerable crossover in both strategies, with 12.5% in the group only culprit injury, and 9.4% in the multivessel group. It is also observed the absence of the option of surgical revascularization, a modality indicated in 36% of the patients in the Shock study.

Although with limitations and criticism, the CULPRIT-SHOCK study is the best evidence available in the therapeutic context of cardiogenic shock. The fact is that its results should have repercussions on the recommendations of the guidelines, indicating a strategy not to be used: complete percutaneous revascularization by visual estimation of the residual lesions in the index procedure. The authors had merit in allowing the indication of staged angioplasty guided by symptoms or presence of ischemia, without considering this procedure as a cardiovascular outcome in the statistical analysis, approach that approaches the real world and the current state-of-the-art in the treatment of coronary artery disease (ischemia driven revascularization).

We can thus conclude that in the case of a patient with cardiogenic shock secondary to acute coronary syndrome, in the presence or not of ST segment elevation, the best initial therapeutic option is to approach only the artery with culprit lesion. If improvement of hemodynamic instability (excluding other shock-perpetuating factors and aetiologies, evaluating symptoms and FFR/iFR ischemia, and pondering the patient's neurological status) is not observed during the evolution, percutaneous intervention of residual lesions should be performed as soon as possible. In patients who evolve with resolution of cardiogenic shock, FFR functional evaluation of the remaining lesions is recommended after clinical stability. In the presence of functionally significant lesions or symptoms, percutaneous treatment should be considered before hospital discharge (Figure 1).

Finally, this study allows us to reflect on some pertinent questions: 1) the high mortality related to ACS complicated with shock, in spite of the evolution of the therapy in the last 20 years; 2) the need for prospective randomized studies that direct us on issues that still rest on evidence of poor quality or expert opinion.

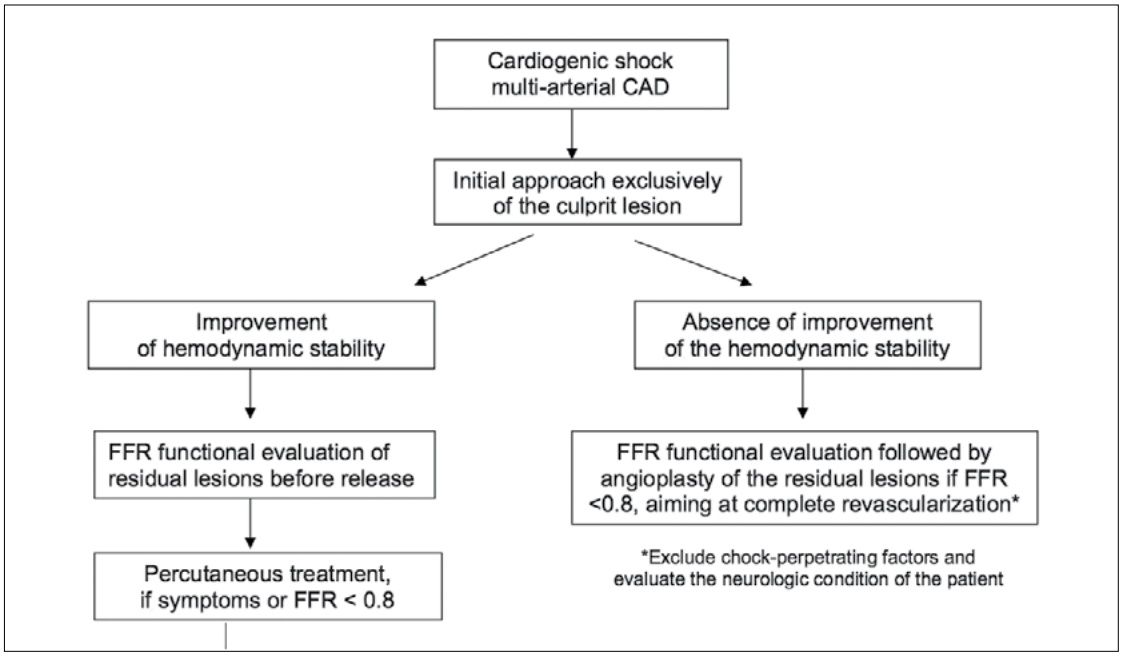

FIGURE 1: Therapeutic approach to cardiogenic shock secondary to acute coronary syndrome in a patient with multivessel coronary artery disease (CAD).

RESUMO

O tratamento de pacientes com infarto do miocárdio com elevação do segmento ST concomitante à presença de doença multiarterial tem sido estudado em vários estudos recentes com o objetivo de definir a necessidade, bem como o melhor momento, de abordagem das lesões residuais. No entanto, tais estudos incluíam apenas pacientes estáveis. A melhor abordagem terapêutica do choque cardiogênico secundário à síndrome coronariana aguda, no entanto, ainda permanece controversa, havendo porém recomendação de especialistas para uma revascularização que inclua as lesões não relacionadas ao evento. Publicado recentemente, o estudo CULPRIT-SHOCK mostrou benefício da abordagem inicial apenas da lesão culpada pelo evento agudo, perante a intervenção percutânea multiarterial, no contexto do choque cardiogênico. No presente ponto de vista, os autores discutem o trabalho em questão, no que concerne a questões metodológicas, limitações e aplicabilidade clínica.

PALAVRAS-CHAVE: *Infarto do miocárdio. Choque cardiogênico. Intervenção coronária percutânea.*

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