Despite all the advances in acute myocardial infarction (AMI) treatment, cardiogenic shock (CS) is still the leading cause of mortality among AMI patients admitted to the hospital (1). Most of the deaths occur within the first 30 days, about half within the first 48 hours (2,3). Although total mortality has decreased, recent trends point to an increase in hospital mortality (4).

Patients with AMI and CS have a baseline risk profile that is usually worse when compared to those without shock. They are older, have a higher frequency of renal impairment, previous myocardial infarction and multivessel coronary artery disease than patients without CS, with significant stenosis in addition to the culprit lesion (5-7). Immediate percutaneous coronary intervention (PCI) of the culprit lesion is the unique therapy associated with proven benefit in reducing mortality, but immediate PCI of both culprit and non-culprit lesions is a matter for discussion. Although European and American guidelines had favourable recommendations to multivessel PCI (8,9), the results of the Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) randomized controlled trial, in which 706 CS patients were assigned to either immediate culprit lesion-only PCI or multivessel PCI, evidenced better outcomes at 30 days with culprit lesion only PCI (10). In that study, the authors observed a lower risk of the composite outcome of mortality or severe renal failure leading to renal-replacement therapy: 45.9% vs. 55.4%, which corresponds to a number needed to treat of 11 (10). The evidence led to a downgraded recommendation of immediate multivessel PCI to class IIIB in the European Guidelines (11).

Among 30-day survivors, long-term mortality rates are also observed to be higher in patients with AMI complicated by CS than in patients without shock (7,12,13). The short-term benefit of culprit-lesion-only PCI over complete revascularization through multivessel PCI may not be sustainable on long-term, and there was even a hypothesis that multivessel PCI could be associated with diminished risk during the longer-term course. Therefore, reliable evidence on long-term outcomes is warranted.

The publication by Thiele et al. in the New England Journal of Medicine shows the result of one-year outcomes for the CULPRIT-SHOCK trial (14). As expected, repeated revascularization was performed more often with the immediate culprit-lesion-only PCI than with the multivessel PCI strategy (32.3% vs. 9.4%; relative risk, 3.44; 95% CI, 2.39 to 4.95). Was this associated with worse outcomes in culprit-lesion-only PCI group? This does not seem to be the case. The analysis of the original primary outcome (composite of mortality or renal replacement therapy) was evaluated in a post hoc analysis at one year, and showed benefit for the culprit-lesion-only PCI strategy: 52.0% of the patients in the culprit-lesion-only PCI group vs. 59.5% in the
multivessel PCI group (relative risk, 0.87; 95% CI, 0.76 to 0.99). When considering the results of overall mortality (30-day mortality and 30 days to one year-mortality), there was a non-significant difference between point estimates (50.0% vs. 56.9%), and the confidence interval for the relative risk points out to a trend of benefit of culprit-only PCI strategy (relative risk 0.88; 95% CI, 0.76 to 1.01) (14). The sample size in the CULPRIT-SHOCK trial was calculated for the 30-day analysis of the primary composite outcome. To use of a composite endpoint is a common strategy to reduce sample size in trials, and it has been widely employed in cardiovascular clinical trials (15). However, the study might not be sufficiently powered to assess each outcome individually, and this may affect the significance of the results. Cardiovascular deaths had occurred in 46.2% of patients in the culprit-lesion-only PCI group and in 52.8% of patients in the multivessel PCI group (relative risk, 0.88; 95% CI, 0.75 to 1.02). The trend may indicate a potential benefit of culprit-lesion-only PCI, which would be significant with a larger sample size. However, as early mortality risk is too high, the analysis of overall mortality may not be an appropriate estimate for mortality after the early phase. In order to investigate mortality before and after 30 days, the authors used landmark analysis, a methodology which has shown to be of interest in cardiovascular research recently. It ignores all events occurring before the landmark time to assess the long-term outcomes, in order to “estimate in an unbiased way the survival probabilities in each group conditional on the group membership of patients at the landmark time” (16). Using landmark analysis, the authors observed that although mortality was lower in the culprit lesion-only PCI group during the first 30 days (relative risk, 0.84; 95% CI, 0.72 to 0.98), it was similar in the two groups thereafter (relative risk, 1.08; 95% CI, 0.60 to 1.93) (14). The results suggest that after the initial benefit of immediate culprit-lesion-only PCI, the results between 30 days and one year are equivalent. As stated by the authors, with regards to multivessel PCI, “the short-term risks that are associated with longer procedure times, more complex initial interventions, and higher doses of contrast material seem to outweigh any potential benefits associated with reducing the subsequent risk of repeat revascularization”.

Those results are in line with polled evidence from nonrandomized studies: a recent systematic review observed that short-term mortality was lower in patients who underwent immediate culprit-only PCI when compared to those treated by multivessel PCI (7 studies, 5,656 patients, 28.8% vs. 37.5%, P=0.001), but long-term mortality did not differ between groups (7 studies, 1,893 patients, 41.7% vs. 44.7%, P=0.77) (17).

Although renal failure was worrisome in the multivessel PCI in short-term related to higher doses of contrast use, no significant difference in renal-replacement therapy was found between the two approaches at one year. It is worth mentioning that the confidence interval shows a trend of benefit (relative risk 0.71; CI, 0.49–1.03) of culprit-only PCI strategy. Trials are usually not sufficiently powered to assess harm, but this result may suggest that culprit-only PCI strategy may decrease the risk of renal replacement therapy. This topic should be a matter of investigation in future studies, adequately powered for this outcome. As chronic kidney failure, even without the need for replacement therapy, is associated with poorer outcomes, it should be a matter of investigation as well (14).

An unexpected finding of the trial was that patients who underwent immediate culprit-lesion-only approach had a higher rate of rehospitalization for heart failure than the ones treated with multivessel PCI (5.2% vs. 1.2%). The authors had two hypothesis to explain this: the higher rate of complete revascularization in the multivessel PCI group than in the culprit-lesion-only PCI group could be associated with subsequent improved ventricular function and a lower subsequent incidence of heart failure; or it could be a consequence of competing risks. The CS patients who did not die early could might have survived to develop heart failure in the longer-term course (14).

The authors highlighted lack of blinding as a potential limitation for the study. As they are dealing with hard outcomes, lack of blinding could influence management and thus downgrade the strength of evidence (18), but it does not invalidate the results. It is also worth mentioning the lack of the randomization property being a limitation for landmark analysis. (16). For this study specifically, a substantial and unbalanced proportion of patients died at 30 days, and prognosis characteristics of the members of forming groups at landmark is different. In this case, although patient characteristics at 30 days was not shown, we could hypothesize that patients from the multivessel PCI group who survived the early phase may have better prognosis characteristics, so the limitation also does not invalidate the results.

According to Ocam’s Razor, as applied to modern Medicine, “simpler solutions are more likely to be correct than complex ones.” Unless immediate multivessel PCI proves to be beneficial, it is better to opt for the simpler strategy, culprit-only PCI.
Acknowledgements

Funding: AL Ribeiro was supported in part by the Brazilian research agencies CNPQ (bolsa de produtividade em pesquisa 310679/2016-8 and IATS 465518/2014-1) and FAPEMIG (Programa Pesquisador Mineiro PPM-00428-17).

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References


Cite this article as: Marcolino MS, Ribeiro AL. Culprit-only or multivessel PCI in cardiogenic shock myocardial infarction patients: simpler solutions are more likely to be correct than complex ones. J Thorac Dis 2019;11(Suppl 9):S1296-S1298. doi: 10.21037/jtd.2019.04.80