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Cardiogenic shock: approaching the truth

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Cardiogenic shock (CS) is a severe clinical condition characterized initially by reduced cardiac output with abnormal organ perfusion which commonly leads to a multiorgan failure. Despite expansion of cardiac critical care units, development of reperfusion networks and progress of mechanical circulatory support (MCS), mortality of CS due to acute myocardial infarction (AMI) remains as high as 40%–50%.[1] Clinical outcomes in non-AMI patients are less established but remains similarly disappointing.[2] Significant areas of uncertainty still remain regarding clinical profile, risk stratification and management of these complex patients. This special issue about CS covers the most important topics assessed by several of the most important experts in the field.

In general, the diagnosis of CS can be made on the basis of clinical criteria in addition to biochemical and hemodynamic parameters. However, the pathophisiology of CS is complex and heterogeneous, and patients may present in different stages, depending on shock severity. Therefore, an early risk stratification is a key issue in order to select patients for invasive procedures such as MCS and to help physicians to predict its evolution. Recently, Baran, *et al.*[3] proposed a new and simple classification based on severity of CS, with five categories form pre-shock to refractory CS labelled as A through E (SCAI stages). Importantly, Jentzer, *et al.*[4] retrospectively validated the SCAI classification for predicting in-hospital mortality in a cohort of more than 10,000 patients admitted because of CS. The role of biomarkers on CS risk stratification has been extensively studied. CardShock[5] and IABP-SHOCK II[6] scores include only classical biochemical parameters, which can take time to change their values and therefore delay clinical decisions. Other biomarkers (i.e., neutrophil gelatinase-associated lipocalin, plasma cystatin C) have not been shown to add value in risk stratification.[7] Proteomics is a promising tool for improving risk prediction in this complex setting. The CS4P score is based on circulating levels of four novel biomarkers (liver fatty acid binding proteins, beta 2-microglobulin, fructose-bisphosphate aldolase B and complement inhibitor). Importantly, when compared to the CardShock and IABP-SHOCK II scores, CS4P showed better ninety-day mortality prediction and a benefit in reclassifying patients.[8] In this special issue, Iborra-Egea, *et al.*[9] discuss the potential clinical implications and translation into clinical practice of this very promising tool.

Clinical picture of CS patients is very heterogeneous. Despite AMI is the most common cause of CS in most registries, non-ischemic CS is an interesting clinical condition with scarce clinical evidence. Fulminant myocarditis is a not uncommon cause of CS that can be due to several diseases, potentially requiring different diagnostic approaches and clinical management. In an interesting review, Montero, *et al.*[10] discuss the main challenges regarding diagnosis and management of this amazing entity, including the potential role of endomyocardial biopsy and the selection of patients for MCS.

On the other hand, the incidence of CS complicating AMI ranges between 3% and 13%.[11] An early revascularization is the only therapeutic measure that has consistently shown a prognostic impact in patient with AMI-CS. In the SHOCK trial, the mortality rates at six months and at one year were significantly lower in the revascularization cohort in comparison with the medical therapy group. Little

evidence exists regarding the role of revascularization in AMI-CS due to left main occlusion. In this setting, the myocardium at risk can be very extensive and a greater number of complications and worse prognosis may occur. In an interesting review, Galván-Román, *et al*.[12] discuss the current literature about this topic, highlighting the high mortality of these patients, the significant heterogeneity and limitations of most studies and the need for larger, specifically designed studies to fully address this clinically relevant question.

MCS devices have emerged during the last decade as one of the most promising tools for the management of critical patients with refractory CS. However, corrent evidence has significant limitations and the high incidence of MCS-related complications difficult to obtain a consistent prognostic benefit in this complex setting. Large trials powered for efficacy and safety are lacking in CS.[13,14] Despite these lack of data, various studies showed a clear increase in the use of these devices.[15,16]

One of the most widely used MCS tools are the Impella devices.[17] These devices have attractive properties such as a minimally invasive insertion, the ability to provide cardiac output for supporting the failing heart, and to unload the left ventricle, in contrast to other devices. In an interesting article, Barrionuevo-Sánchez, *et al*.[18] describe the potential contribution of the Impella devices at different stages and clinical settings of CS.

On the other hand, despite the widespread of mechanical reperfusion has reduced the incidence of mechanical complications in AMI, these clinical conditions still occur especially in cases with late diagnosis or unsuccessful reperfusion. Surgical correction is the only effective treatment in most cases. However, a significant proportion of patients are denied surgery in routine clinical practice because of high surgical risk. In this sense, MCS (especially venoarterial extracorporeal membrane oxygenation) can allow an early stabilisation in order to achieve surgery in a more estable condition. In an interesting review, Rob, *et al*.[19] analyze the potential contribution of MCS in AMI-CS, especially focusing in patients with mechanical complications. The main conclusions from Rob, *et al*.[19] are the need for tailoring device selection according to the cause and severity of CS, an early MCS initiation and multidisciplinary team cooperation and the importance of ongoing prospective randomized trials for optimizing MCS indications, timing, and patient selection.

Finally, the lack of robust evidence regarding the management of patients with CS is mostly due to the inherent problems from performing randomized clinical trials in this critical scenario. Factors such as shock severity, cardiac arrest or age make it difficult to design these trials when determining eligibility criteria. Moreover, ethical issues often pose a major challenge for inclusion. In an excellent article from this special issue, Freund, *et al*.[20] review the difficulties we may encounter in the randomized controlled trials design and propose some recommendations to solve them.

In conclusion, the information included in this special issue may contribute to a better description of the clinical profile of CS patients and an improvement of risk stratification and clinical management of a pathology with an unacceptably high mortality. This information may also give some clues about where future research in this area should focus.

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