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EDITORIAL COMMENT

Mitral Regurgitation in Cardiogenic Shock

A Novel Target for Transcatheter Therapy?*

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Cardiogenic shock (CS) remains one of the most serious diagnoses in clinical medicine with mortality rates up to 50% even in the context of clinical trials (1). In recent years, the field has seen advancements in the management of patients with acute myocardial infarction-associated CS including early revascularization of the culprit artery by means of percutaneous coronary intervention (1), but also major drawbacks such as the lack of benefit of intra-aortic balloon counterpulsation in randomized clinical trials (2). Increasing efforts are made to implement a multidisciplinary team-based approach in specialized centers and state-of-the-art practice standards to improve care for patients with CS (3). Still, all too often, we have our backs against the wall and long for additional therapeutic options while trying to stabilize patients in this highly acute and complex illness.

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Severe mitral regurgitation (MR), a potentially treatable condition, is observed in about 10% of patients with acute myocardial infarction-associated CS (4,5) and has been associated with higher 1-year-mortality (4), but similar in-hospital-mortality (5) when compared with CS patients without severe MR. Valid conclusions on the clinical risks and benefit of MR reduction by transcatheter mitral valve repair (TMVr) in these patients have been hampered by the lack of appropriately sized cohorts. In this issue of *JACC: Cardiovascular Interventions*, Jung et al. (6) report on a pooled patient-level analysis of previously published case series and studies, investigating the outcome of 141 patients with CS and moderate-to-severe MR undergoing mitral valve edge-to-edge repair with the MitraClip device (Abbott Vascular, Santa Clara, California). In these patients, predominantly presenting in Society for Cardiovascular Angiography and Interventions (SCAI) CS classes C and D, TMVr itself was safe without procedural complications. MR reduction to grade 2 or less was achieved in about 89% of patients. On the basis of the available data, such MR reduction was hemodynamically well tolerated, and no acute deterioration in left ventricular (LV) function was evident. In-hospital mortality in the entire cohort was 15.6% and lower than expected, considering the distribution of SCAI CS classes. Of note, patients in whom MR was successfully reduced displayed lower in-hospital and 90-day mortality when compared with patients without MR reduction following TMVr.

Considering the lack of effective therapeutic alternatives in these patients, Jung et al. (6) have to be congratulated for their analysis because it is the first to provide a more solid database for further evaluation of the potential benefit of TMVr in CS. As is often the case, cutting-edge papers leave us with more questions than answers. For the paper by Jung et al., such questions relate to at least 3 critical aspects of TMVr in CS, that is, patient selection, timing of intervention, and impacts on hemodynamics.

With regard to patient characteristics, the principal causes of CS as well as the volume status and hemodynamic phenotype (i.e., ventricular preload, volume, and systemic vascular resistance) at hospital admission remain unknown. Patients were in advanced age and had several comorbidities. Therefore, not only ischemic events were likely causative for the initiation of CS in this pooled cohort, but also other trigger factors such as heart rhythm disorders, infections, worsening renal function, or in fact,

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progressive valvular disease. About one-quarter of patients presented with degenerative MR or mixed MR etiology, but we do not learn in how many patients MR was acute or chronic with acute deterioration. As can be inferred from the baseline characteristics, the patient cohort was rather heterogeneous with 80% of patients having had a history of heart failure, and it is rather likely that these patients had some degree of pre-existing MR. We believe that the etiology and initial presentation of CS, as well as the extent of pre-existing right and left ventricular impairment, MR, and pulmonary vascular remodeling, are critical determinants of the benefit of TMVr in these patients. Future studies are undoubtedly needed to address these factors in more detail, because they are important to ensure reasonable progress for this novel and very specific application of TMVr.

Importantly, from a hemodynamic point of view, forward failure was likely not the main reason to consider TMVr in the analysis by Jung et al. (6). Certainly, despite a time lag between hospital admission and intervention, the majority of patients were still on inotropes, and one-third of patients received mechanical circulatory support. Yet, mean arterial blood pressure was controlled, LV ejection fraction and cardiac index were reduced, but not excessively low, and glomerular filtration rate was ≥60 ml/min in 60% of patients. On the contrary, pulmonary and right atrial pressures were elevated, and 36% of patients were intubated, arguing for refractory congestion as a more relevant issue to consider TMVr in these patients. This notion is further supported by the fact that heart failure medication was already re-established in a substantial number of patients. On the basis of the very preliminary data currently available, we may speculate that following initial stabilization, there are patients with CS and persistent backward failure sustained by moderate-to-severe MR, where TMVR not only enhances decongestion and further weaning of inotropic support, but also improves in-hospital and short-term outcomes. However, whether such a strategy is superior to intra-aortic balloon counterpulsation or other mechanical circulatory support devices is currently completely unknown, making it even more important for upcoming studies to define and investigate subgroups among CS patients with the highest likelihood of TMVr success based on clinical or hemodynamic characteristics.

Clearly, a major concern about TMVr in these patients is the risk of afterload mismatch, that is, further acute impairment of LV systolic function due to increased afterload following reduction of the low-impedance mitral regurgitant flow. In patients without CS, a transient afterload mismatch resolving before hospital discharge has been observed following TMVr (7), and data from cardiac magnetic resonance studies in patients at markedly increased surgical risk suggest that TMVr not necessarily results in immediate improved cardiac output and effective biventricular forward flow despite marked MR reduction (8). Although LV ejection fraction decreased by 4% on average following TMVr in the present study, the investigators did not report any acute deterioration in LV function. However, we need to be cautious not to underestimate the potential risks of afterload mismatch in this patient population, particularly because these patients were on inotropic or mechanical circulatory support, and this may have blunted a worsening of LV systolic function in response to the sudden increase in afterload following TMVr.

Hence, although we are eagerly waiting for novel therapeutic approaches to improve the often dramatic clinical course and poor prognosis of patients in CS, we need to accept that it is too early to draw any firm conclusion on a potential benefit of transcatheter treatment of MR in CS. For sure, the findings by Jung et al. (6) are encouraging and should stimulate more intense research in the field, but there is still a long way to go. Let`s hope TMVr finally finds a role in CS management, in the interest of our patients.

AUTHOR DISCLOSURES

Dr. Lurz has been a consultant to and has received speaker honoraria from Abbott. Dr. Besler has reported that he has no relationships relevant to the contents of this paper to disclose.

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