[Cardiogenic Shock 1]

Optimal use of Various MCS in the field of Cardiac Critical Care

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Mortality for cardiogenic shock remains elevated, and the only therapy that has shown to improve survival in a acute myocardial infarction-related cardiogenic shock (AMI-CS) is early revascularization, as demonstrated by the SHOCK trial, as well as revascularization of culprit-only revascularization in patients presenting with AMI-CS and multivessel coronary artery disease, as demonstrated in the CULPRIT-SHOCK trial. However, other studies assessing the use of vasoactive medications, including vasopressors and inotropic agents, have not demonstrated any difference in survival between treatment arms. Similarly, randomized clinical trials of mechanical circulatory support (MCS) devices have failed to demonstrate improvement in mortaltiy with these devices, including intra-aortic balloon pump (IABP), as shown by the IABP-SHOCK II trial, as well as veno-arterial veno-arterial membrane oxygenation (VA ECMO) as demonstrated by the ECMO CS and ECLS SHOCK trials, that were recently published. Similarly, other small underpowered studies comparing temporary percutaneous LVAD (e.g. Impella) have also failed to demonstrate superiority over other forms of MCS. Notably, while these trials deserve major credit for its completion and for addressing such key investigational questions, in a condition where it is extremely challenging go complete RCTs, it is important to understand the patient population included in the trails and how to integrate such key information provided by these very well conducted RCTs into clinical practice.

For instance, published studies so far have only included patients with AMI-CS, while those with other etiologies of CS, such as acute on chronic heart failure, myocarditis, valular heart disease and others, limiting the applicability of the RCTs findings to such patient population. This is particularly important as AMI-CS constitutes only about 30% of the patients of the patients currently admitted with CS to the cardiac intensive care units in the United States, and with similar proportions to those admitted in Europe. Moreover, in addition to differences in etiology of CS, it is important to appropriately classify CS according to its phenotype, including severity of shock by using SCAI SHOCK stages or other risk scores (e.g. IABP SHOCK II score or CardShock score), ventricular involvement (right, left or bi-ventricular shock), organ perfusion and congestion (non-congested, cardio-renal or cardiometabolic) and hemodynamic profile (e.g. classic, vasodilatory and/or normotensive shock). Hence, the appropriate phenotyping and understanding of patient's presentation, is key for selection of therapies and monitoring strategies, including medications, invasive versus non-invasive monitoring and MCS devices. Therefore, the implementation of a goal-directed, holistic and multi/interdisciplinary approach, with shock teams and shock algorithms, is key to improve outcomes in cardiogenic shock.

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What We Have Learned from Observation Studies and Clinical Trials in CCCTN

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The field of critical care cardiology has significantly grown in the last few decades, and has rapidly evolved as a result of the growing complexity of the patients admitted to the contemporary cardiac intensive care units. This transition from the "coronary care unit" to the "cardiac intensive care unit" has underscore the importance of the integration of cardiovascular medicine and critical care medicine in order to best incorporate intensive care concepts tailored to the specific pathophysiology of the critically ill cardiac patient. Therefore, the current practice of critical care cardiology has evolved and adapted to meet these demands, including ongoing discussion about needs to better understand the optimal strategies for staffing, training, credentialing, networking and academic development in critical care cardiology. Moreover, as critical care cardiology sets itself apart as a distinct subspecialty, there has been a pivotal need to provide high quality data and evidence-based recommendations that are specific and tailored to the contemporary CICU. This has led to the development of the Critical Care Cardiology Trials Network, which is a collaborative research network that includes key opinion leaders from the United States and Canada in critical care cardiology, and that is coordinated by the TIMI Study Group. The CCCTN main objective is to design and execute observational studies and clinical trials that will advance the care of the critically ill cardiac patient.

The CCCTN has provided key evidence to understand the contemporary demographics and treatment patterns in level 1 CICUs, including a specific characterization of the diagnosis, disease severity, resource utilization, demographics and other key data in the current practice of

critical care cardiology. Similarly, it has allowed us to better understand the specifics of cardiogenic shock features, from clinical presentation to specific hemodynamics, as well as risk stratification, phenotyping, device utilization and outcome data. It has also provided key information regarding non-cardiac conditions complicating admissions to the CICU, including respiratory failure, renal dysfunction, end-of-life issues and others. The CCCTN network has also allowed the execution of clinical trials including the CCCTN COVID-PACT clinical trial and other ongoing studies. To date, CCCTN has included over 40,000 patients with key granular data and with strict data collection criteria, making it the most important and largest database in critical care cardiology created to date. In summary, CCCTN serves as a unique tool to enhance evidence-based practice of critical care cardiology.