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EDITORIAL

Potential growth in cardiogenic shock research though an international registry collaboration: the merits and challenges of a *Hub-of-Spokes* model

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Cardiogenic shock (CS) due to an acute myocardial infarction (AMI) is a high acuity condition associated with significant morbidity and mortality.[1] Over the past 2 decades, only 11 major randomized trials have been published with enrolment modestly ranging from 40 to 706 patients.[2] Despite advances in early invasive revascularization and culprit-only percutaneous coronary intervention (PCI), mortality rates remain 30–50%.[3–6] These poor outcomes coupled with a small number of trials relative to other cardiovascular conditions highlights the remaining significant knowledge-treatment gaps in this population. In this special CS-themed issue of *EHJ: Acute Cardiovascular Care*, investigators used existing clinical trial datasets and registries to advance understanding of four major areas related to the CS epidemiology and management: (i) initial risk assessment; (ii) emergency revascularization; (iii) timing of mechanical circulatory support (MCS), and (iv) end-organ complications.

Initial recognition and risk assessment of emerging CS is a fundamental goal of care of these patients. Rivas-Lasarte *et al.*[7] leveraged the 5-center Red-Shock cohort in Spain to externally validate the IABP-SHOCK II (AUC 0.742) and CardShock (AUC 0.752) scores. The findings that both scores had good discrimination reassures clinicians that the scores can be used to aid with in-hospital prognostication. However, an important distinction is that no CS models have been validated for MCS or for withdrawal-of-life-sustaining-therapy decisions. International professional society guidelines recommend early invasive evaluation of patients with CS due to AMI. Josiassen *et al.*[8] studied 1716 patients who underwent angiography for CS at 2 Danish centres finding 56% with multi-vessel disease. A left main culprit lesion was frequently associated with multi-vessel disease and was independently associated with 30-day mortality (Hazard Ratio 1.42, 95% CI 1.07–1.86) raising concern regarding outcomes with contemporary management of these patients and the question whether future studies should test whether complete emergency surgical revascularization is a better approach than culprit-only PCI in this high-risk subgroup. Optimal strategies for MCS in the setting of AMI-CS also remain uncertain. Fuernau *et al.*[9] analysed the intra-aortic balloon pump (IABP)-SHOCK II trial database to compare survival between pre- (12%) and post-PCI IABP placement. The authors reported no difference in 30-day (Odds Ratio 0.99, 95% CI 0.47–2.12) or 1-year mortality. The rationale for this analysis includes prior observational data suggesting that left ventricular unloading with microaxial MCS pre-PCI may improve outcomes compared with post-PCI implantation.[10] The reported point estimates suggest that the neutral results of the main IABP-SHOCK II trial are independent of implantation timing, though this secondary analysis likely lacks statistical power. Finally, end-organ complications of CS are a major driver of outcomes. Renaudier *et al.*[11] retrospectively analysed data from initiation of extra-corporeal membrane oxygenation (EMCO) (65 patients post-cardiotomy, 85 with CS, and 39 with cardiac arrest) in a single centre to describe a 9% prevalence of mesenteric ischaemia (diagnosed a median of 4 days after ECMO initiation) associated with a 100% mortality rate. The study highlights the challenge with recognizing lactic acidosis as a marker of regional mesenteric ischaemia in the setting of global hypoperfusion and that re-establishment of systemic flow does not negate the risk of end-organ hypoperfusion; though it should be acknowledged that the lack of pathology precludes discriminating embolic from non-obstructive mesenteric ischaemic.

While each of these studies brings new knowledge, they highlight a common limitation. Cardiogenic shock registries and trials are small and underpowered compared with contemporary cardiovascular mega-trials focused on AMI, heart failure, dyslipidaemia, and/or diabetes. Enrolment in CS trials is complicated by a smaller pool of patients, inherent time sensitivity for treatments in deteriorating patients, communication barriers like mechanical ventilation[6] and

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sedation, and comorbidities (such as cardiac arrest) that may limit survival. Overcoming these challenges may require innovative and pragmatic modifications to existing silos of CS research. We propose collaboration to create a common 'network of networks' CS registry (*Figure 1*) wherein existing successful (spoke) registries[7,12–14] would contribute data to a common dataset (hub). Expert, industry, and regulatory stakeholders have emphasized a need for large CS registries and a platform for registry-embedded clinical trials[15]; a cooperative pathway would mitigate the challenges of creating new registry infrastructure, leverage the strengths of existing networks, allow for continued quality improvement feedback to participating sites, and create a dataset suitable for retrospective analysis. Moreover, an ancillary benefit of such an endeavour is that it would also facilitate harmonization of acuity staging, definitions of CS, and complications. A common language and data elements could help mollify the current difficulties with inter-registry comparisons of incidence, outcomes, and/or quality-of-care. Such a proposed strategy would face challenges including: (i) the need to define data governance, (ii) establishing equitable criteria for authorship of scientific output, (iii) overcoming barriers to seamless data transfer, (iv) navigation of international rules for data privacy, (v) implementation of common practices for data acquisition and quality, and (vi) creating partnerships for sustained funding.

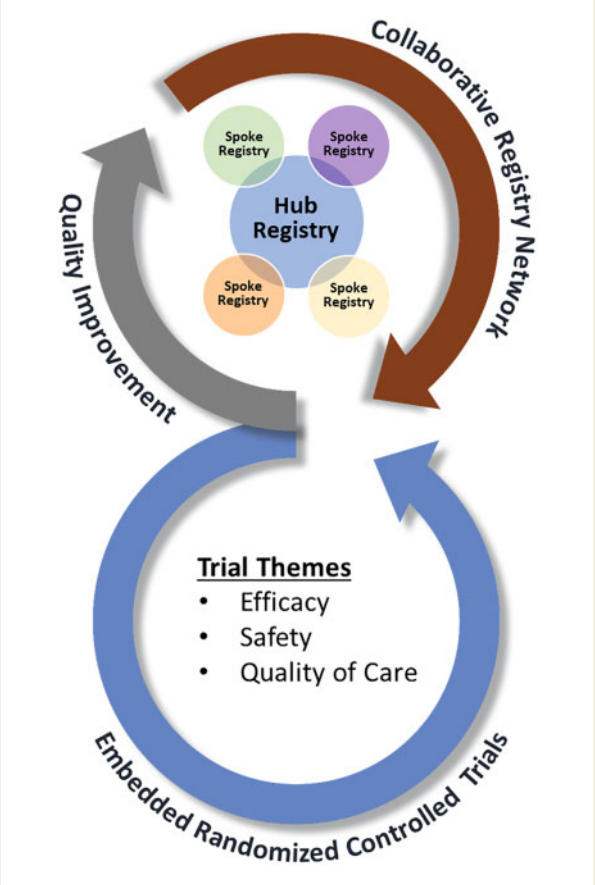

Figure 1 Potential role of a collaborative *hub of spokes* registry to serve as framework for registry enable trials and quality improvement feedback.

Ongoing effort to create common definitions and data elements for studies of CS will be invaluable in creating a foundation for data-sharing and coalescence of large datasets.[15] As well, advancing approaches to extraction of data from electronic health records and interoperability frameworks between existing data sources will accelerate progress towards the goal of efficient data collection and sharing. International collaboration supported by cardiovascular professional societies, particularly in the area of acute cardiovascular care, will foster engagement of necessary stakeholders and provide opportunities for regional comparative analyses that may lead to new insights into variability in care and develop evidence to establish best practices.

The persistently high mortality rates in CS call for multidimensional interventions that may include improvements in public health education, prognostication, clinical care, MCS technologies, strategies to mitigate complications, and regional systems of specialized care. There is currently a renewed CS research interest and with multiple ongoing modestly sized randomized trials of MCS technologies, we may be on the precipice of advancement, but our collective CS efforts still lag (in size and number) behind the benchmarks set by other cardiovascular conditions. Innovation through transformation of traditional registry models to facilitate larger international collaborations may help address existing knowledge-treatment gaps to improve survival in this high acuity condition.

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