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Editorial

Don't go breaking my. . .lungs? The acute respiratory distress syndrome is common, deadly, and probably underrecognized after cardiac arrest

The acute respiratory distress syndrome (ARDS) is a heterogenous clinical syndrome characterized by lung injury related to a local or systemic insult leading to acute hypoxemia and radiographic opacities.[1] Fifty-five years after ARDS was first described by Drs. Ashbaugh and Petty, clinicians and scientists are still working to fully elucidate its heterogenous pathophysiology, test specific therapeutics, identify clinical risk factors, and most importantly, prevent its development.[2,3] A number of "traditional" ARDS risk factors have been identified, but cardiac arrest is not listed among them.[4]

In this issue of Resuscitation, Shih and coauthors add to the growing literature highlighting that ARDS is common after cardiac arrest and may be associated with worse outcome.[5] They present a retrospective cohort analysis of 203 patients who suffered in-hospital cardiac arrest (IHCA) from 2014 to 2018 and sustained return of spontaneous circulation. Key among their reported findings are the following: 72% developed ARDS within 3 days, and those with ARDS had fewer alive-and-ventilator free days and higher hospital mortality compared to those without, though these differences did not persist after adjustment with a multivariable model.

A previous study conducted by our group demonstrated comparable findings in a cohort of out-of-hospital cardiac arrest (OHCA) patients.[6] In 600 mechanically ventilated patients who suffered OHCA and survived for 48 hours, 50% developed ARDS. ARDS was associated with higher hospital mortality, longer ICU stay, more ventilator days, and lower incidence of neurological recovery. The lower incidence of ARDS in our study compared with Shih et al. likely reflects the underlying conditions that contribute to out-of-hospital versus in-hospital cardiac arrest, different time windows in which development of ARDS was evaluated, and the slightly discrepant definitions used in each study. Both studies clearly highlight that ARDS is a major problem in the post-arrest population that warrants further study.

Patients who suffer cardiac arrest often have numerous "traditional" risk factors for ARDS, including aspiration, chest wall and lung parenchymal trauma, and pulmonary infection.[7] It remains unknown, but plausible, whether ischemia and reperfusion following cardiac arrest may contribute, as it does in other conditions such as lung transplantation.[8] Some of these risk factors might represent specific clinical phenotypes that lead to opportunities for understanding pathophysiologic mechanisms and identification of therapeutic targets. For example, prophylactic antibiotics have been demonstrated to reduce the incidence of early-onset ventilator pneumonia after OHCA, a major risk factor for ARDS.[9]

We posit that cardiac arrest should indeed be included among ARDS risk factors with the goal of raising awareness among clinicians and further highlighting important research gaps. In fact, given the multitude of potential insults, ARDS following cardiac arrest may even be *more common* than is seen with "traditional" ARDS risk factors.[4] With the high prevalence of ARDS, one may reasonably ask whether all post-arrest patients should be managed with lung-protective ventilation. Ventilation with low tidal volumes, a proven strategy for ARDS with a 9% absolute mortality reduction, has been demonstrated to improve outcome after OHCA, but not IHCA, a discrepancy which merits further study.[10–12] We believe clinicians should vigilantly monitor for the development of ARDS, however, widespread, prophylactic adoption of lung protective ventilation in these patients could result in more ventilator dysynchrony, more sedative exposure and greater hypercapnia, which could impact neurological prognostication and outcomes. Some data suggest, however, that mild permissive hypercapnia is beneficial after cardiac arrest; a definitive, phase 3 randomized trial just completed enrollment.[13–16]

This study has limitations. It was conducted at a single center, has a limited sample size, and began enrolling patients in 2014. The relatively small number of patients enrolled likely limited the authors' abilities to detect differences in their adjusted primary outcome, alive-and-ventilator free days. While the older data set raises some question about whether cutting-edge ARDS or cardiac arrest therapies were used, a more contemporary data set might be even more problematic as the COVID-19 pandemic has dramatically changed the epidemiology of both in-hospital cardiac arrest and ARDS.[17,18]

Much work remains. First, we must work to better understand the impact of ARDS on cardiac arrest outcomes. Extracerebral organ dysfunction remains a major contributor to morbidity and mortality and likely impacts decisions to provide or withdraw life sustaining therapy.[19] Second, we must elucidate the pathophysiology of post-arrest ARDS, including disentangling the complex interplay between hydrostatic lung edema and endothelial and epithelial lung injury. Then, we must identify biological phenotypes and targets for pharmacologic interventions and other novel therapies.[20] Fourth, we must further develop strategies to prevent ARDS in this high-risk population. These may include novel approaches to airway

decontamination, temporary mechanical circulatory support and selective perfusion, and cocktails aimed to mitigate the effects of ischemia–reperfusion injury. In closing, improving how we care for these fragile patients will require research and strategies to mitigate multiorgan injury balanced with the imperative to optimize neurological outcomes.

Conflict of Interest Statement

The authors report no conflicts of interest.

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NJJ was lead author on a similar publication focused on out-of-hospital arrest, published in Resuscitation: Johnson NJ, Caldwell E, Carlbom DJ, Gaieski DF, Prekker ME, Rea TD, Sayre M, Hough CL. The acute respiratory distress syndrome after out-of-hospital cardiac arrest: Incidence, risk factors, and outcomes. Resuscitation. 2019 Feb;135:37-44. PMID: 30654012.

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