Variation in the Incidence and Timing of Acute Lung Injury

The Role of Race

Over the past decade, the scientific community has gained a deeper understanding of the epidemiology of acute lung injury (ALI) and ARDS. Several high-quality studies have provided estimates of the incidence of ALI/ARDS, and have shown how incidence varies by age and what predicts mortality in this disease.^{1,2} Our understanding of how race/ethnicity influences an individual's risk of developing ALI, however, is much less clear. Past population-based studies that characterized the incidence of ALI were conducted in geographic regions that did not reflect the typical racial/ethnic diversity of the United States, which prevented the presentation of race-specific estimates.^{1,2} At least one study of all-cause respiratory failure that included patients with ALI suggested that black patients experience a higher incidence of ALI.³ However, the *International Classification of Diseases, Ninth Revision*-based definition of respiratory failure used in this study left open the possibility that the observed racial differences in respiratory failure were due to causes other than true ALI. Most experts speculate that black patients are at an increased risk of developing ALI largely because black patients are at greater risk of sepsis and pneumonia,^{4,5} the two most common causes of ALI. In addition, several studies demonstrated that black patients die of ALI in greater numbers but appear to experience only slightly greater mortality once acquiring ALI, compared with white patients.^{6,7} Perhaps the most plausible explanation for the results of these studies is that the greater number of deaths due to ALI among black patients is most attributable to a higher incidence.

In this issue of *CHEST* (see page 901), Lemos-Filho and colleagues⁸ provide data that challenge this assumption. The authors examined >5,000 participants enrolled in a multicenter cohort study designed to characterize the predictors of ALI among those hospitalized with established ALI risk factors. This unique at-risk population allowed the authors to compare the percentage of patients who eventually developed ALI

across race, sex, and age groups. The strengths of the study included the prospective (most centers) collection of data, the use of the consensus definition for ALI, the diversity in the sites participating in the study, and a rich collection of information on each individual allowing adjustment for differences across race groups. Consistent with past studies, the risk factors of sepsis and pneumonia were more common among black compared with white patients. Somewhat surprisingly, even contradictory to most racial disparities work, black patients were less likely to develop ALI compared with white patients. Of those at risk, 6.5% of white patients and only 4.5% of black patients developed ALI, a finding that persisted after adjustment for other patient differences across race groups.

Given the greater rates of sepsis and pneumonia among black Americans, both in this study and in the population, why then are black patients less likely to develop ALI? Through their careful analysis, the authors were able to exclude several potential explanations. First, the authors appropriately adjusted for race-based differences in the prevalence of diabetes across race groups, a comorbidity that may reduce the risk of ALI.⁹ Second, the authors adjusted for tidal volume delivered to patients before ALI was present. It is becoming increasingly recognized that lower tidal volumes may protect individuals who are mechanically ventilated from developing ALI.¹⁰ Third, the authors also appropriately accounted for center effects in their analysis. An extensive body of literature now demonstrates that a minority of hospitals care for the majority of black patients.¹¹ If the hospitals where black patients seek care provide higher-quality care, black patients on average would develop ALI less often. Yet the race-based differences in the current study were observed despite conditioning on hospital (ie, the relationship between race and the development of ALI was the same for each hospital included in the analysis).

There is at least one important explanation for the lower risk of ALI among black patients that Lemos-Filho and colleagues⁸ were unable to address. Specifically, 35% of patients with ALI ($n = 166$) were given a diagnosis of ALI at hospital admission and, per the study protocol, these individuals were excluded from data extraction, preventing the authors from characterizing the racial makeup in this group. If the

percentage of black patients in this excluded group was greater than that in the study sample, it is possible that the lower risk of developing ALI among black patients may not result from a true difference in the incidence of ALI, but rather from a difference in the timing of incident ALI. In other words, many of the incident cases of ALI in black patients may have already occurred by the time of hospital admission but were excluded by design. Indeed, past studies suggest that black patients often present to health-care providers later in the course of their critical illness, resulting in greater severity of illness at the time of admission.^{5,7} Had the authors been able to include the group of patients with early ALI in their analysis, one can only speculate as to how the relationship between race and ALI would change. Nevertheless, the possibility that differences in the occurrence of ALI across race groups may be a function of timing suggests that further studies are needed and leaves open the possibility that the population-based incidence of ALI in black patients may be equivalent to or even greater than that of white patients,³ even if the hospital-based incidence is lower.

Racial disparities in medicine are pervasive and continue to exist despite decades of effort to eradicate them.¹² As we seek to further address such disparities through research, many health disparities experts argue for a moratorium on studies that aim to document the existence of racial disparities. Instead, they suggest that investigators focus on determining the mechanisms underlying disparities or on interventions to remediate them. The study by Lemos-Filho et al⁸ provides a nice countervailing point to this argument, demonstrating why descriptive work is still important: On occasion, the results of such studies may surprise us.

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Joining the Crowd

Cystic Fibrosis and Cardiovascular Disease Risk Factors

Numerous chronic inflammatory diseases that activate systemic inflammatory biomarkers, such as periodontitis,¹ HIV,² inflammatory bowel disease,³ rheumatoid arthritis,⁴ and even psoriasis,⁵ are reported to be associated with an increased incidence of cardiovascular disease (CVD). Respiratory tract (RT) diseases are among this roster of chronic inflammatory diseases. These include COPD,⁶ α_1 -antitrypsin deficiency,⁷ and possibly adult-onset asthma.^{8,9} Might cystic fibrosis (CF) join the crowd?