Pulmonary Congestion in Hemodialysis: An Old Chestnut Worth Screening For?

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It is well documented that pulmonary congestion is common among patients undergoing treatment with hemodialysis, and recent evidence suggests a strong association with mortality (1–4). The cyclical, and very predictable, nature of each hemodialysis session carries several major risks that may compromise cardiorespiratory function and threaten the patient's well-being (5). One major consequence is the accumulation of fluid during the interdialytic period, which has a propensity to collect in the lungs and lead to progressive pulmonary congestion, particularly among patients with compromised left ventricular function (1). Although the pathogenesis of this process is generally well understood and the inevitable consequences are obvious, our ability to effectively diagnose and treat this common condition has been less than satisfactory, exposing patients to unnecessary and potentially lethal clinical consequences (6). Pulmonary congestion that becomes clinically apparent from symptoms of shortness of breath prompts the clinical team to conduct a rapid set of clinical investigations and follow through with a personalized treatment strategy. Changes in the dialysis treatment prescription such as increased ultrafiltration, provision of extra dialysis treatments, re-evaluation of a patient's dry weight, and a cardiac assessment are some of the recognized treatment practices that may be required. Pulmonary congestion that is not clinically apparent to the team or indeed the patient presents an even more challenging scenario (7,8). This "silent" pulmonary congestion by its very nature is difficult to detect, develops insidiously, and poses a serious threat to patient welfare.

In this issue of *CJASN*, Enia and colleagues (9) provide a novel and unique perspective into the association of pulmonary congestion with physical functioning in hemodialysis. Using data from a multicenter study of 270 Italian hemodialysis patients, they describe for the first time an independent and inverse association of pulmonary congestion with impaired physical functioning measured before hemodialysis treatments. The primary exposure, pulmonary congestion, was assessed by chest ultrasonography, which measures the amount of extravascular water that accumulates in the lung from the thickness of the interlobular septa (1). The extent of water accumulation in the lungs was calculated by a cumulative score that indicated the thickness of the interlobular septa. Physical performance assessment was based on self-report using the physical functioning scale of the Kidney Disease Quality of Life Short Form (KDQOL-SF).

There are three major findings that merit discussion in this editorial. First, 58% of hemodialysis patients in this survey had evidence of moderate to severe lung congestion before each hemodialysis session, whereas almost 40% of these patients had apparently no pulmonary symptoms. As a practicing clinical nephrologist, one must be alarmed at the observation that almost two thirds of patients have moderate to severe pulmonary congestion before a hemodialysis treatment at a time when classic thrice-weekly hemodialysis remains the "gold" standard prescription for most hemodialysis programs. Assuming good external validity, one might also infer that most patients in standard hemodialysis programs are in a perpetual state of central volume overload that possibly begins soon after a hemodialysis treatment and progressively worsens before the next treatment. There is an increasing body of evidence that supports the finding of excessive fluid gains with elevated mortality (1–4,10). Indeed, Zoccali and colleagues recently demonstrated the independent prognostic effect of severe pulmonary congestion on all-cause and cardiovascular mortality in a multicenter prospective cohort study (10). The risk of all-cause death increased >4-fold, whereas that of fatal and nonfatal cardiovascular events increased >3-fold. These data highlight the detrimental effect of pulmonary congestion on clinical outcomes among maintenance hemodialysis patients and our inability to effectively manage them as we continue with conventional hemodialysis treatment practices.

A second, and equally noteworthy finding, was the strong correlation of pulmonary congestion with poorer physical functioning before hemodialysis treatment. Regardless of age, coexisting cardiovascular comorbidity, and several nutritional markers, the greater the degree of pulmonary congestion before hemodialysis, the higher the probability of poor physical functioning. For many readers, it may not be surprising to learn that overt pulmonary congestion was linked with poor patient physical performance and indeed, one might have expected to see the graded effect of increasing pulmonary congestion with reduced physical functioning. What was surprising was the complete lack of association of commonly measured nutritional and

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metabolic indicators of health with poor physical functioning in the adjusted analysis. It is possible that this may relate to the performance characteristics of the KDQOL-SF because it does not capture quantitative performance such as cardiorespiratory fitness, which may be related to nutritional parameters (11). Nevertheless, the KDQOL-SF, adapted for use in the Italian dialysis population (12), is a validated metric for capturing physical functioning in hemodialysis, and is a strong determinant of morbidity and mortality (13).

Third, and even more striking, was the finding of lower physical functioning among the subgroup with asymptomatic pulmonary congestion. The relationship between symptomatic central fluid overload and poor physical performance could well have been expected. Patients with the most severe physical symptoms based on New York Heart Association class had the poorest physical performance and this was confirmed in multivariable analysis. However, the discovery that patients who had sonographic evidence of pulmonary congestion but without symptoms and had equally poor physical performance sheds new light on its importance. This study would suggest that asymptomatic pulmonary congestion is a distinct clinical entity with measurable consequences. Indeed, asymptomatic pulmonary congestion explained 16% of the variability in impaired physical functioning.

The findings from this study raise important questions on the value of chest ultrasonography in routine assessment of volume status among patients undergoing maintenance hemodialysis. Equally important, these results raise significant concerns regarding the current clinical practice of thrice-weekly hemodialysis for volume control in this high-risk population. This Italian study demonstrates that the standard practice of clinical volume assessment and management is suboptimal in contemporary hemodialysis cohorts. A large percentage of patients had moderate to severe pulmonary congestion before hemodialysis treatment based on a validated ultrasonography technique. Equally worrisome is the observation that many patients receiving hemodialysis treatment have ultrasonographic evidence of pulmonary congestion, but this does not come to the attention of the clinical team because these patients are completely asymptomatic.

This study is not without limitations. The study design was cross-sectional and consequently limits causal inference, and thus one cannot state with any degree of certainty that pulmonary congestion led to the development of poor physical functioning. One might also criticize the self-report measure of physical functioning that was utilized from the KDQOL-SF 36 and perhaps its lack of specificity for quantitative physical performance measures (11). For example, to what extent does a self-report instrument capture other components of physical functioning and physical fitness (*e.g.,* muscle strength, cardiorespiratory fitness)? Indeed, the lack of association of nutritional and metabolic indicators with physical functioning in this study may reflect this limitation. Nevertheless, its validity as a physical functioning metric has been well established in large-scale epidemiologic studies in the nephrology literature (13). The characteristics of the population were representative of a predominantly European dialysis population, with an average age of 66 years and a 28% prevalence of diabetes, although it will be necessary to validate these findings in racially and ethnically diverse non-European populations.

To what extent can this new-found information advance the practice of hemodialysis and improve volume management in at-risk patients? Although there are a number of methods for estimating volume status in day-to-day clinical practice, the nephrology team has traditionally depended on noninvasive clinical methods such as the standard clinical examination, measurement of interdialytic weight gains, and relative plasma volume monitoring (14). With advancements in chest ultrasonography, it should be possible to routinely screen for pulmonary congestion with greater precision before dialysis treatment. This critical piece of information is likely to be more important to clinical decision making than measurement of interdialytic weight gains. Indeed, the authors found little correlation between pulmonary congestion using chest ultrasonography and interdialytic weight gain, suggesting that interdialytic weight gain is a poor substitute for central volume assessment.

Going forward, it will be important to explore whether the application of chest ultrasonography in routine clinical practice will alter our decision-making capacity and lead to improved volume control among hemodialysis patients. At the very least, it should stimulate an amplified response to tackle the high rates of pulmonary congestion as suggested in this study, especially if the findings are confirmed in demographically and racially diverse populations. Increases in the frequency of hemodialysis or/and the duration of treatments are the likely downstream consequences, and these strategies were shown to be beneficial in improving patient outcomes (15). Volume assessment and its management among patients undergoing hemodialysis may be viewed by some as the Achilles heel of dialysis practice. Excessive volume gains during the interdialytic period predict increased mortality risk and now reduced physical functioning. The advent of chest ultrasonography may herald a new approach to volume assessment and control. Earlier recognition, detection, and quantification of extravascular lung water should provide the nephrology team with new practical information to inform decision making and guide prescribing practices, with the potential to affect major clinical outcomes. Randomized controlled trials are now required to test whether screening for pulmonary congestion in hemodialysis patients leads to better volume control, reduced cardiovascular events, and improved patient survival and quality of life. This approach may herald the dawn of a new era and a paradigm shift in managing central fluid overload in hemodialysis.

Disclosures

None.

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