Symposium 7.1
Heart and Kidney: an insidious relationship

Lung congestion in chronic kidney failure

Carmine Zoccali, Italy

Despite many available dialysis-related performance measures, there is still none addressing fluid volume and cardiac status. The available fluid volume indicators, such as symptoms, vena cava diameter, and radio-isotopic methods, are either unreliable or impractical. The body impedance assessment (BIA) is the most commonly used measure of whole-body fluid, but it does not provide insight into a fluid burden in the lungs. Lung ultrasound (LUS) has recently emerged as a possible objective measure of fluid overload in dialysis patients.

The optimal fluid volume depends on extracellular fluid volume and cardiac function, which is represented by left ventricular (LV) filling pressure. LV filling pressure is a surrogate measure of LV preload and operating compliance and corresponds to the alveolar capillary pressure. High pulmonary capillary pressure increases extravascular lung water, which can be detected by the presence of comet-tail artifacts (the so-called B-lines) on the LUS image. The number of B-lines is proportional to alveolar capillary pressure and the degree of lung congestion.

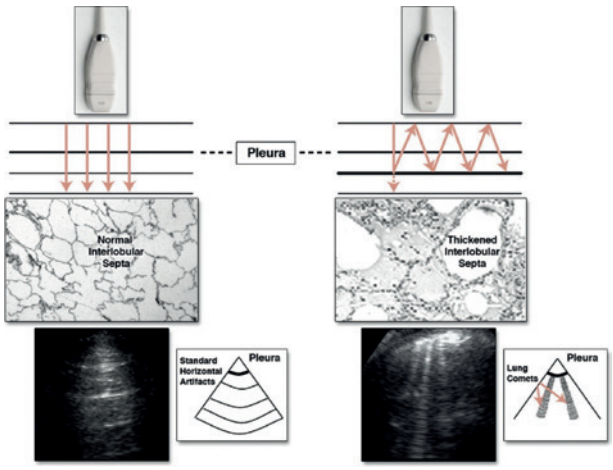

Figure 1.
Ultrasound in normal lung and pulmonary congestion: the image from the normal lung surface contains horizontal A-line artifacts, while the so-called B-lines indicate the presence of interstitial edema (from ref. 1)

Early detection of pulmonary congestion is of fundamental importance in dialysis patients. One of the first studies evaluating LUS as a tool for early diagnosis of fluid overload in the dialysis population found that the vast majority of hyperhydrated dialysis patients were completely

asymptomatic. The number of B-lines poorly correlated with hydration status measured by BIA, suggesting that the crucial factor underlying lung congestion was LV dysfunction and LUS was able to capture this congestion at a pre-clinical stage. Furthermore, pulmonary congestion in hemodialysis patients was strongly and independently associated with cardiac events and mortality.

A recent international, multi-center randomized controlled trial investigated whether an LUS-guided treatment strategy improved a composite endpoint (all-cause death, non-fatal myocardial infarction, decompensated heart failure) vs usual care in patients receiving chronic hemodialysis with high cardiovascular risk. Three hundred and seven patients completed the study, 152 in the active and 155 in the control arm. During a mean follow-up of 1.5 years, lung congestion was significantly more frequently relieved in the active than in the control arm and the intervention was safe. The primary composite endpoint, the risk for all-cause and cardiovascular hospitalization, and the changes in LV mass and function did not significantly differ between the groups. Thus, in patients on chronic hemodialysis with high cardiovascular risk, a treatment strategy guided by LUS effectively relieved lung congestion but was not more efficient than usual care in improving the overall outcomes. A larger trial focusing on decompensated heart failure in hemodialysed patients is still needed to validate the value of LUS in this population.

The importance of screening and assessment of kidney function in patients with heart failure and DM2

Martin de Borst, Netherlands

Effective screening strategies contribute to earlier disease detection ensuring timely treatment initiation, better disease control, and fewer or delayed complications. Unlike certain other diseases with established screening programs, there is still no consensus on whether health systems should prioritize early identification and intervention for chronic kidney disease (CKD), even though this condition does meet the World Health Organization principles for screening.

Type 2 diabetes (T2D) and heart failure patients are at high risk for developing CKD. The prevalence of proteinuria in these populations is 32% and 33% respectively and reaches 56% in individuals with combined conditions. Nevertheless, according to the latest reports relying on data from very large international cohorts, only 35% of T2D patients and merely 4.1% of hypertensive patients are screened for albuminuria, and there is no data whatsoever for individuals with heart failure. Furthermore, screening was largely unrelated to the predicted risk of prevalent albuminuria. Nevertheless, there is strong evidence that the addition of creatinine-based eGFR and albumin-to-creatinine ratio significantly improves the discrimination of cardiovascular outcomes beyond traditional risk factors in the general population, especially in individuals with T2D or hypertension.

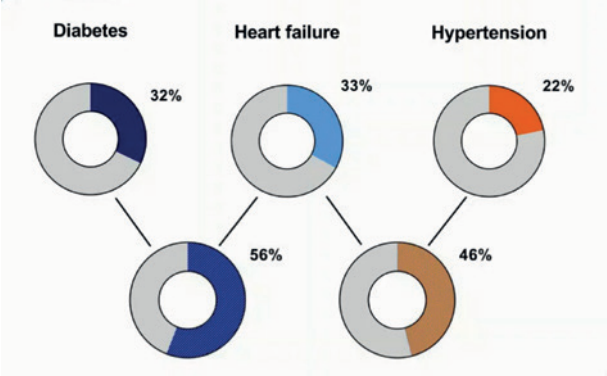

Figure 2.
Prevalence of increased albuminuria in high-risk populations (based on ref. 6)

There are currently several lines of therapy available for patients with diabetic CKD. The choice is guided by the level of eGFR and the presence of albuminuria, thus presenting yet another argument for albuminuria screening in this population. Nevertheless, the cost-effectiveness of such a measure is still open to debate, even though large systematic reviews report results in favor of screening. The latest guidelines support this strategy and suggest at least annual eGFR and albuminuria assessment in T2D patients.

As for the patients with heart failure, the added benefit of albuminuria measurement might be less compelling since the treatment for the underlying disease is in line with measures directed at albuminuria. Nevertheless, this population could still benefit from the periodic assessment of kidney function.

Uremic cardiomyopathy – is it truly reversible by transplantation?

Charles Ferro, United Kingdom

Uremic cardiomyopathy represents cardiac remodeling that occurs in CKD patients and is associated with high morbidity and mortality rates in this population. Even though the links between kidney disease, left ventricular hypertrophy and heart failure were recognized as early as the

19th century by Richard Bright, this particular finding was described 50 years ago. The current understanding of uremic cardiomyopathy describes the condition as a unique cardiovascular phenotype characterized by progressive heart muscle disease, increased arterial stiffness, atherosclerosis, and hypertension appearing early in CKD and progressing to diastolic and systolic dysfunction and myocardial fibrosis in end-stage kidney disease. Endomyocardial biopsies in hemodialysis patients with dilated cardiomyopathy without coronary artery disease revealed severe myocyte hypertrophy and interstitial fibrosis which was strongly associated with cardiac mortality. Non-invasive cardiac assessment with magnetic resonance (CMR) imaging using gadolinium to identify the presence of myocardial fibrosis identified two main myocardial pathologies in this population. Left ventricular hypertrophy was the predominant cardiomyopathy specific to uremia, while left ventricular dilation and systolic dysfunction were related to underlying ischemic heart disease. More recent studies used measurement of native T1 through CMR to avoid concerns related to gadolinium and nephrogenic systemic fibrosis in dialysis patients.

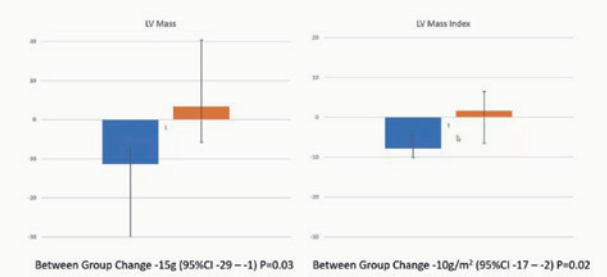

Figure 3.
Changes in left ventricular mass 12 months after transplantation (blue boxes) and in controls (orange boxes)

It was common grounds that these severe functional abnormalities of the heart could be reversed following transplantation. However, this idea relied on the results from small, opportunistic, and uncontrolled echocardiographic studies that were perpetuated in later review articles. A recent systematic review and meta-analysis challenged these assumptions by revising all studies published from 1950 to 2020 that evaluated left ventricular systolic and diastolic function with imaging modalities before and after renal transplantation. The review found poor methodological quality of evidence and no support for the belief that uremic cardiomyopathy is reversible by renal transplantation. These conflicting results urged the initiation of a prospective study of the effects of transplantation on CKD-associated cardiomyopathy using magnetic resonance imaging which started in 2018. It aimed to recruit 55 transplanted patients and 30 controls to detect a change in left ventricular fibrosis following kidney transplantation using T1 mapping CMR. The study was heavily impeded by the outbreak of COVID19, but the preliminary results show a significant decline in left ventricular mass one year after transplantation. Further research is expected to provide more evidence on this issue.

Further readings

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All the speakers reviewed and approved the content.