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The Interconnectivity of The Cardio-Renal-Metabolic Systems and Associated Comorbidities

### Announcer:

You're listening to ReachMD. This medical industry feature is titled "The Interconnectivity of The Cardio-Renal-Metabolic Systems and Associated Comorbidities." Here is your guest, Dr. Pam Kushner.

### Dr. Kushner:

Welcome everyone and thank you for listening today as we discuss the final topic in our heart failure podcast series. My name is Dr. Pamela Kushner, I am a clinical professor at the University of California at Irvine Medical Center, a clinical trialist, past chair of the American Academy of Family Physicians Drugs and Device Committee and a Family Medicine Doc with a private practice in Long Beach, California

Last time, my colleague discussed the updated 2022 joint guideline for the treatment of heart failure from the American College of Cardiology, American Heart Association, and the Heart Failure Society of America. Today, we will discuss the cardio-renal-metabolic, or CRM, systems and their interconnectivity. We will also discuss important and common comorbidities of heart failure patients.

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I'd like to begin today by introducing and discussing the CRM systems. The CRM systems are physiologically interconnected, and each one relies on energy homeostasis to function properly.

The heart and the kidney are two of the most metabolically demanding organs of the body, requiring large amounts of oxygen and fuel to support their various specialized functions.

In fact, the renal system functions together with the cardiovascular and metabolic systems to regulate hemodynamics such as volume homeostasis and blood pressure, as well as to facilitate the reabsorption and transportation of glucose.

Meanwhile the cardiovascular system functions together with the metabolic and renal systems to regulate metabolic activities and maintain homeostasis.

Due to this interconnectivity, disorders of these 3 systems frequently occur in combination.

If we look closely at cardiovascular disorders, for example, we see that cardiovascular comorbidities are highly prevalent in patients with type 2 diabetes. In fact, up to 45% of patients with heart failure also have diabetes. This is not surprising because diabetes is associated with multiple risk factors that can predispose patients to heart failure and atherosclerosis.

Unfortunately, patients with heart failure and type 2 diabetes often have a poor prognosis and a 4 times greater likelihood of experiencing heart failure-related hospitalizations compared to those without type 2 diabetes. Further, each hospitalization increases the morbidity and mortality of the patient going forward.

There also are other comorbidities that occur within the CRM continuum.

For example, patients with diabetes who have decreased glucose oxidation and increased levels of free fatty acids, can exhibit lipid accumulation and lipotoxicity.

Often forgotten is diabetic cardiomyopathy, which is characterized by cardiomyocyte hypertrophy and is the result of impaired calcium

handling in cardiomyocytes, as well as mitochondrial dysfunction and increased oxidative stress. Studies have shown that cardiomyocyte hypertrophy may result from insulin resistance and cell growth in response to hyperinsulinemia. Excess angiotensin II and aldosterone production can also induce cardiomyocyte hypertrophy and fibrosis. Together, all of these conditions contribute to the pathogenesis of the disease.

All of these examples further highlight the interconnectivity of the CRM systems and the importance of understanding their interplay to help improve the lives of patients.

Turning back to the kidney, heart failure can also lead to progression of hypoperfusion, apoptosis, and fibrosis within the kidney, with more than 60% of patients with heart failure having progressive kidney disease.

When an individual has heart failure, the heart cannot meet metabolic requirements and is unable to accommodate systemic venous return. Compensatory mechanisms to restore this cardiac output include increased venous pressure, sympathetic nervous system activation, and natriuresis, resulting in worsening kidney function.

The kidney will then promote renin-angiotensin-aldosterone system activation, which includes sodium and water retention and vasoconstriction, resulting in worsening heart failure. Therefore, one of the roles of renin angiotensin receptor antagonists as among the pillars of therapy in the previously reviewed guidelines

In patients with type 2 diabetes, the primary focus for disease management has been on CRM conditions. Not only are these comorbidities both prevalent and prognostically important but they also substantially impact treatment choices and should be considered together.

Thank you all for joining me today.

As we have discussed, the CRM systems are physiologically linked and the relationships between these systems is complex. Understanding the CRM continuum is vital for healthcare professionals to effectively treat heart failure comorbidities, such as type 2 diabetes.

I hope from this heart failure podcast series, you've learned more about and grown to appreciate the complex clinical nature of the disease. Heart failure is the most rapidly growing cardiovascular condition in the United States and remains a significant burden to patients, caregivers, providers, and healthcare professionals. Understanding how to accurately diagnose early heart failure and its associated comorbidities, as well as increasing disease state awareness will have a positive impact on patients and their caregivers. Additionally, adherence to guideline-directed medical therapy for the management of heart failure will improve the outcomes for patients with this debilitating disease.

**Announcer:**

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