

# The complexity of heart failure



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**H**ear failure is a complex clinical syndrome that is associated with frequent hospitalizations, a poor quality of life, and a high rate of mortality. The prevalence of heart failure is rising in the world, especially heart failure with preserved ejection fraction (HFPEF), which is now the most common type of heart failure.<sup>1</sup> It is becoming increasingly clear that heart failure is not a single entity, but rather a heterogeneous group of pathologies with multiple phenotypes. Heart failure is also often accompanied by a number of comorbidities, including renal failure, diabetes, obesity, lung disease, liver disease, obesity, chronic inflammatory diseases, and thyroid disease. Heart failure itself can also contribute to the severity of these comorbidities. Unfortunately, the pathophysiological relationship between heart failure and these comorbidities is complex and not fully understood.

Obtaining a better understanding of the pathological processes that contribute to heart failure and to the comorbidities that accompany heart failure is critical in order to develop new therapies to treat both heart failure and the comorbidities accompanying heart failure. This issue of *Heart and Metabolism* discusses the complex relationship between the heart failure syndrome and potential accompanying comorbidities. It also addresses novel treatment options for heart failure therapy, including those that target the treatment of peripheral organ diseases.

An understanding of the interaction between the heart and other peripheral organs is critical in the

optimal tailoring of heart failure therapies. The article by **Agata Bielecka-Dabrowa, Breno Godoy, Maciej Banach, and Stephan von Haehling** addresses the interaction between the kidney, liver, pancreas, skeletal muscle, lungs, and thyroid gland with the heart in mediating heart failure severity. It also nicely highlights how targeting these peripheral organs (ie, such as in cardiorenal syndromes) can be used to successfully treat heart failure. The article by **Gopinath Sutendra and Evangelos D. Michelakis** also describes the interaction of the lung with the development of heart failure, particularly in the setting of pulmonary arterial hypertension. It highlights the importance of considering right ventricular failure in describing heart failure syndromes. It is also clear that treatments targeting other diseases can also affect the severity of heart failure, which is evident in the article by **Oliver J. Müller and Lorenz Lehmann** that demonstrates the potential of cancer chemotherapy in producing cardiotoxicity and increasing heart failure severity.

Understanding the link between heart failure and other comorbidities can provide potentially new avenues for treating heart failure. The article by **Edoardo Bertero and Christoph Maack** highlights some of the new approaches that may soon be available to treat heart failure, including therapies originally targeted toward treating diabetes, which may also lessen heart failure severity. Heart failure is also associated with dramatic alterations in cardiac energy metabolism (see the Refresher Corner article by

Gary Lopaschuk) that can also be potentially targeted to treat heart failure. In support of this, the article by Mario Marzilli highlights how targeting cardiac energy metabolism is a novel approach to treating heart failure. This metabolic approach to treating heart failure may also be useful in treating right heart failure, as discussed in the article by Gopinath Suttendra and Evangelos D. Michelakis). Combined, it has become clear that heart failure should not be considered in isolation, but rather in the context of

the relationship between the heart and other associated comorbidities. In this regard, optimal therapy of heart failure would ideally involve both the direct treatment of heart failure as well as the treatment of any associated comorbidities. ■

## REFERENCES

1. McHugh K, De Vore AD, Wu J, et al. Heart Failure with preserved ejection fraction and diabetes. *J Am Coll Cardiol.* 2019;75(5):602-611.