

Renal failure and takotsubo syndrome: the chicken and the egg

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Cardiorenal syndrome (CRS) represents a clinical entity that covers a broad spectrum of diseases associated with chronic or acute involvement of both the heart and kidneys.¹ CRSs may present with 2 possible clinical conditions, cardiorenal and renocardiac CRS, based on the *primum movens* of the disease (cardiac or renal). Both cardiorenal and renocardiac CRSs are then divided into acute and chronic, according to the onset of disease. The fifth type of CRS integrates all types of cardiorenal involvement induced by systemic disease.

Takotsubo syndrome (TTS) not rarely encompasses clinical signs of both cardiac and renal failure. In TTS populations, the prevalence of renal failure exceeds 30%. TTS and consequent acute heart failure worsen renal function, and, on the other hand, renal failure may precipitate TTS.^{2,3} TTS and dialysis do not seem to be an uncommon association anymore.⁴

How does TTS lead to renal failure and how does renal failure precipitate TTS? There is substantial evidence for the presence of sympathetic overactivity in patients with dialysis and non-dialysis chronic kidney disease, and sympathetic overtone is known to elicit TTS.⁵ TTS and renal failure may share electrolyte abnormalities.⁶

Is TTS another possible clinical presentation of CRS, as some authors suggest?⁷

In their elegant paper, Zalewska-Adamiec et al⁸ provide further evidence linking TTS and kidney disease: in a cohort of 95 patients with TTS and prevalence rates of chronic kidney disease exceeding 30%, a 3-year follow-up mortality rate reached 33% in the presence of kidney disease. In a multivariate analysis, serum creatinine concentrations were found to be a predictor of long-term mortality.

These very interesting data are in line with previous results showing acutely impaired creatinine levels as predictor of a poor outcome in TTS.² Renal dysfunction was found as indicative

of outcomes in hospitalized patients with TTS.⁹ From this reasonable perspective, TTS may fall within the wider spectrum of heart failure disease, where renal dysfunction represents a well-known predictor of outcome.¹⁰ Even from a wider point of view, the impact of noncardiac comorbidities on TTS is again confirmed. Of 5 TTS patients with in-hospital mortality, 4 had an underlying critical illnesses.¹¹ Secondary forms of TTS, with a stressor represented by exacerbation of a comorbidity like chronic obstructive pulmonary disease or kidney insufficiency, are associated with a worse outcome in short- and long-term follow-up.¹² Other comorbidities described in patients with secondary TTS are neurological disease¹³ or malignancy.¹⁴ Therefore, a wide spectrum of underlying chronic diseases can be present in TTS, dramatically influencing the clinical outcome.

That is what we do know, but there is much more that we do not know! Why TTS patients have a much more higher prevalence of chronic disease when compared with an age-matched population?¹⁵ Which mechanism links TTS, kidney disease, and renal failure? And finally, in the “deadly duet”, what is the chicken and what is the egg? More research is surely needed to more completely understand the pathophysiology of TTS and its link with underlying comorbidities and kidney disease.

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