



# Refractory congestive heart failure: when the solution is outside the heart

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## Abstract

Refractory congestive heart failure is associated with an ominous prognosis in which the treatments strategies remain scarce and not well validated. In the last years, continuous ambulatory peritoneal dialysis (CAPD) has emerged as a therapeutic alternative in this subset of patients. So far, it has been associated with a significant improvement in functional capacity and quality of life, together with a striking reduction in the risk of readmissions. We present the case of an elderly patient with severe left ventricular dysfunction and severe mitral and tricuspid regurgitation who presents recurrent admissions for anasarca. After its inclusion in a CAPD programme, the patient experienced a marked clinical and biochemical improvement despite the persistence of cardiac abnormalities. CAPD onset translates into greater sodium removal. We want to emphasize the usefulness of this therapy in the management of volume excess in patients with refractory heart failure and renal failure promoting a greater sodium removal compared with traditional diuretic strategies.

**Keywords** Peritoneal dialysis; Refractory congestive heart failure; Treatment

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## Introduction

Pulmonary and systemic congestion is the main cause for most of the symptoms and signs of heart failure (HF), being responsible for the majority of readmissions.<sup>1</sup> Diuretics remain the cornerstone of the pharmacological treatment of congestion in HF patients.<sup>1,2</sup> However, as the disease progresses, congestion becomes refractory, despite intensive diuretic therapy, a fact that overshadows the clinical prognosis.<sup>1,2</sup>

In the last years, there is emerging evidence showing that congestion itself, far from being an epiphenomenon, plays a causal role in the progression of the disease.<sup>2–4</sup> For example, the progressive deterioration of renal function frequently seen in these subjects is often due to a rise in venous and intra-abdominal pressures.<sup>2–4</sup> Recently, continuous ambulatory peritoneal dialysis (CAPD) has emerged as a useful new strategy for the management of patients with refractory advanced HF and concomitant renal failure.<sup>5,6</sup> However, the

pathophysiological mechanisms endorsing the utility of this technique in this scenario remain not fully clarified, it appears that ultrafiltration of sodium and water plays a crucial role. In the next case report, we describe the clinical, biochemical, and echocardiographic evolution of a patient with refractory congestive heart failure (CHF) included in a CAPD programme. In this case report, we present new data aiming to unravel the crucial mechanisms under this beneficial effect.

## Case report

We describe the case of a 74-year-old man with a history of hypertension, diabetes mellitus type 2, dyslipidemia, chronic kidney disease secondary to nephroangiosclerosis [estimated glomerular filtration rate (eGFR) around 30 mL/min/1.73 m<sup>2</sup>], and chronic ischaemic heart disease with a double aorto-coronary bypass graft and mitral valvuloplasty in 2012 due

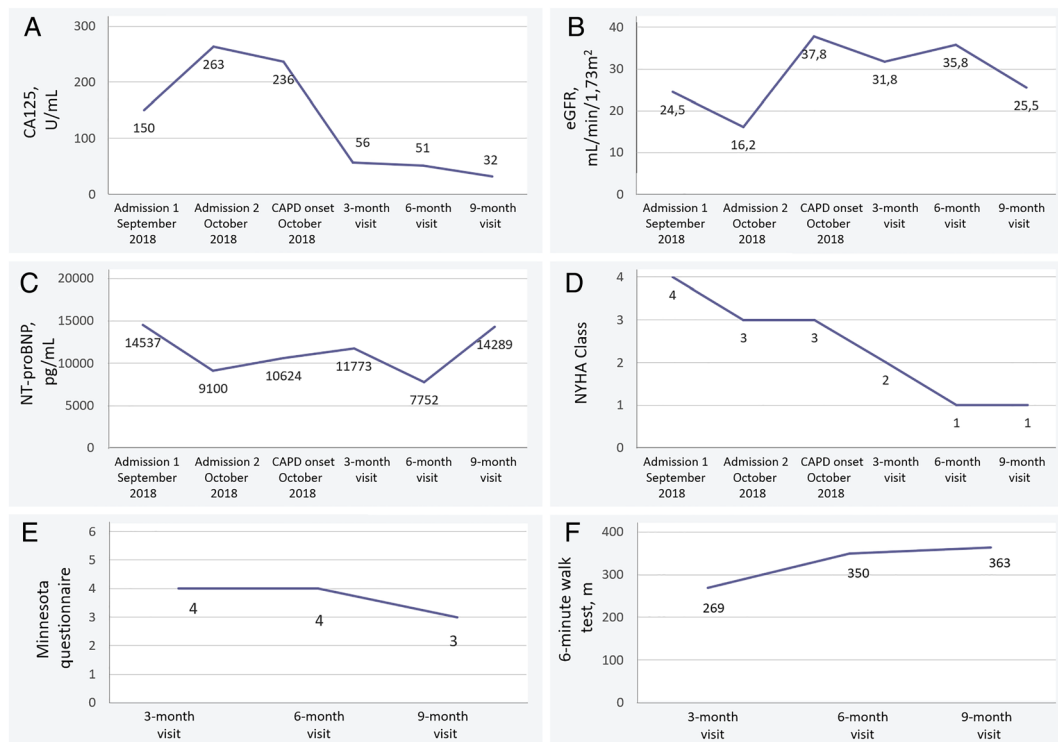
to functional mitral regurgitation. In September 2018, the patient was admitted due to acute heart failure in anasarca situation. Blood test analysis showed an eGFR of 24 mL/min/1.73 m<sup>2</sup> and high values of amino-terminal pro-brain natriuretic peptide (14 537 pg/mL) and carbohydrate antigen 125 (CA125) (120 U/mL) (Figure 1). The transthoracic echocardiogram showed enlarged left ventricle, with severely depressed left ventricular ejection fraction (27%), severe pulmonary hypertension (estimated systolic pulmonary arterial pressure of 65 mmHg), and severe functional tricuspid and mitral regurgitation (effective regurgitant orifice area = 0.54 mm<sup>2</sup>). The patient received intensive diuretic therapy and was discharged 12 days later in functional Class III of the New York Heart Association (NYHA) for outpatient follow-up in the HF unit.

One month later, he was readmitted for acute heart failure despite being under maximized oral diuretic treatment (triple nephron block: furosemide 120 mg/day, chlorthalidone 50 mg/day, and spironolactone 50 mg/day) and intermittent ambulatory administration of intravenous furosemide in HF unit. Given this situation, a percutaneous intervention on the mitral valve (Mitraclip® device) was attempted, but during the procedure, there was a persistence of Grade III mitral regurgitation and appeared

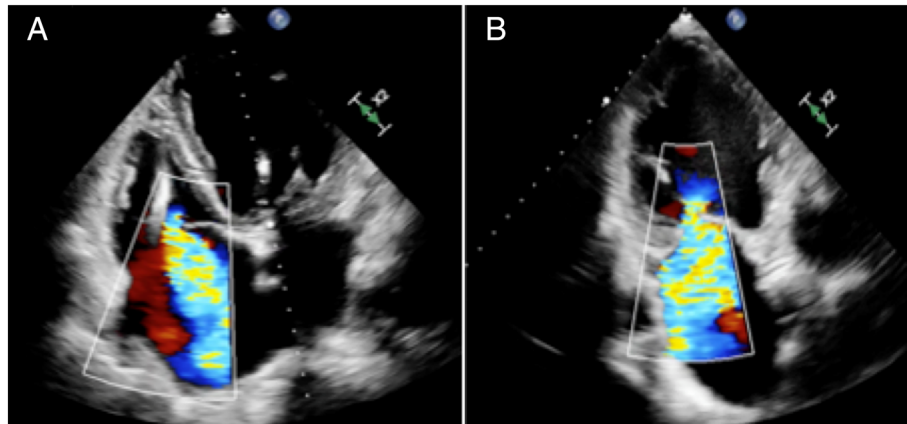
significant mitral stenosis, so it was finally decided not to implant the device. After the failed implant, given the refractory CHF, the patient was included in the CAPD programme. Two weeks after discharge, the abdominal catheter was implanted without complications. Once finished the training period, continuous ultrafiltration was started (two daily exchanges of dextrose solution) with progressive and sustained improvement of congestive signs disappearing lower limbs edema and hepatojugular reflux.

Three months after CAPD initiation, the echocardiographic study showed the persistence of severe left ventricular ejection fraction depression and severe tricuspid and mitral regurgitation (Figures 2A and 2B). In spite of these echo findings, the patient continues experiencing a substantial improvement in NYHA class, congestion parameters, and renal function during the following 8 months (Figure 1). Additionally, the patients showed a progressive improvement in the 6-min walking distance and the Minnesota Living with Heart Failure Questionnaire along the follow-up (Figure 1). At 9-month follow-up, the patient remains in NYHA I class, with no admission or visits to the emergency room. At three different visits, 24-h urine and dialyzed sodium excretion were measured, in every measurement, and despite ultrafiltration volumes ranged from 700 to 1000 mL/day, the 24-h

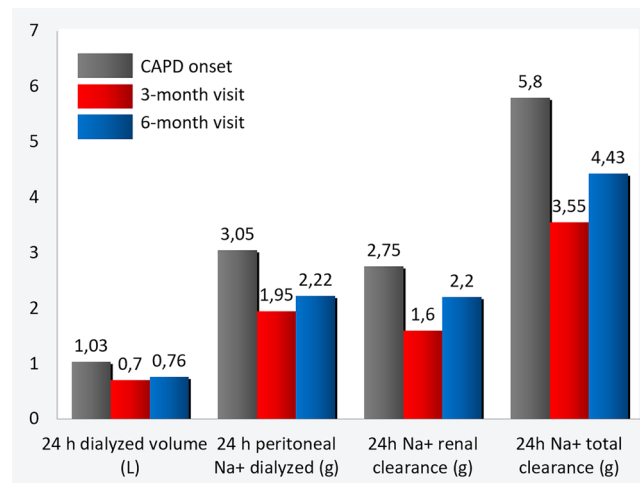
**Figure 1** Temporal evolution of surrogates of the severity of the disease. (A) Antigen carbohydrate 125. (B) eGFR by MDRD formula. (C) NT-proBNP. (D) NYHA class. (E) Minnesota questionnaire. (F) Six-minute walk test. CAPD, continuous ambulatory peritoneal dialysis; CA125, carbohydrate antigen 125; eGFR, estimated glomerular filtration rate; MDRD, Modification in Diet in Renal Disease; NT-proBNP, amino-terminal pro-brain natriuretic peptide.



**Figure 2** Images of the transthoracic echocardiography at 3 months of follow-up after continuous ambulatory peritoneal dialysis onset. (A) Apical view of four chambers showing severe tricuspid regurgitation. (B) Apical view of three chambers showing severe mitral regurgitation.



**Figure 3** Urine, dialyzed, and total sodium clearance. CAPD, continuous ambulatory peritoneal dialysis.



peritoneal sodium excretion exceeded urinary sodium excretion (Figure 3).

## Discussion

Heart failure (HF) is one of the main causes of morbidity and mortality in the elderly population.<sup>2</sup> Many of these patients develop renal failure as the disease progresses, which complicate their management and reduce the therapeutic options, besides accelerating the progression of both diseases.<sup>2,4</sup> The diuretic treatment represents the first therapeutic option to improve the symptoms caused by venous congestion; however, with its chronic use, resistance may appear.<sup>1,2</sup>

Continuous ambulatory peritoneal dialysis (CAPD) in patients with refractory HF and renal failure allows a proper

management of volume excess, because it offers a continuous ultrafiltration, relieves venous and intra-abdominal pressure, and facilitates the elimination of water, in addition to sodium and other solutes (inflammatory cytokines), a fact that is probably associated with a lower activation of the renin-angiotensin system, helping to preserve renal function.<sup>5</sup> In this context, CAPD has been shown to be associated with a significant improvement in functional capacity and quality of life, together with a marked reduction in readmissions in patients with refractory CHF.<sup>6,7</sup> This case, beyond illustrating the usefulness of CAPD in this challenging case of CHF, highlights the importance of optimal decongestive therapy in the course of the disease. Furthermore, this case emphasizes the promising role of CAPD for the treatment of patients with refractory CHF by promoting greater sodium clearance than conventional diuretic strategies.

The patient described presented a very noticeable clinical, functional, and biochemical improvement after initiating CAPD despite persistent ultrasound findings of poor prognosis. Interestingly, despite the fluid removal with CAPD appears not substantial (values ranging from 700 to 1000 mL/day), this was not true for peritoneal excretion of sodium. In fact, the 24-h elimination of sodium by the peritoneum was always higher than observed in the urine.

We believe that the approach of the patient with advanced HF, especially when there is evident data of pulmonary hypertension and right HF, goes beyond a 'cardiocentric' vision. In these patients, we should first focus on volume and sodium excess management. In certain situations, such as the one described, one should look beyond the 'heart' understanding that HF is a systemic syndrome with systemic repercussions. In this case, we illustrated the importance of adequate management of venous congestion in the

modification of progression of the disease. Along this same line, we pointed out the emerging role of CAPD as a depletive strategy promoting a greater sodium removal compared with traditional diuretic strategies. Finally, further studies should confirm the present findings, ideally in a more controlled setting, and also compare the utility of different peritoneal dialysis solutions (dextrose vs. icodextrin) in this particular scenario.

## Conflict of interest

Dr Julio Nuñez and Dr Jose Luis Górriz have received fees for scientific presentations from Vifor and Fresenius Medical Care.

## References

- Mullens W, Danman K, Hajola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WW, Orso F, Rossignol P, Metra M. The use of diuretics in heart failure with congestion - a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2019; **21**: 137–155.
- Ponikowski P, Voors A, Anker S, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2016; **37**: 2129–2200.
- Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, Young JB, Tang WW. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol* 2009; **53**: 589–596.
- Núñez J, Miñana G, Santas E, Bertomeu-González V. Cardiorenal syndrome in acute heart failure: revisiting paradigms. *Rev Esp Cardiol* 2015; **68**: 426–435.
- Grossekkettler L, Schmack B, Meyer K, Brockmann C, Wanninger R, Kreuzer MM, Frankenstein L, Kihm LP, Zeier M, Katus HA, Remppis A, Schwenger V. Peritoneal dialysis as therapeutic option in heart failure patients. *ESC Heart Fail* 2019; **6**: 271–279.
- Núñez J, González M, Miñana G, García-Ramón R, Sanchis J, Bodí V, Núñez E, Puchades MJ, Palau P, Merlos P, Mascarell B. Diálisis peritoneal ambulatoria continua y evolución clínica de pacientes con insuficiencia cardíaca congestiva refractaria. *Rev Esp Cardiol* 2012; **65**: 985–995.
- Núñez J, González M, Miñana G, García-Ramón R, Sanchis J, Bodí V, Núñez E, Puchades MJ, Palau P, Merlos P, Llàcer A, Miguel A. Continuous ambulatory peritoneal dialysis as a therapeutic alternative in patients with advanced congestive heart failure. *Eur J Heart Fail* 2012; **14**: 540–548.