

Comorbid Renal Failure in Heart Failure

JAVIER MARIANI¹

In this issue of the Revista, Acosta et al. present a detailed study about the prevalence of renal failure in a group of patients with heart failure and left ventricular systolic dysfunction. The study shows that moderate levels of renal failure (creatinine clearance < 60 ml/min) are present in more than 40% of patients with chronic heart failure (CHF). (1) Patients with renal failure had less functional capacity, poor nutritional status, and higher biomarker values, and they received evidence-based treatments less frequently than those who did not have renal failure.

Heart failure is a condition that most often affects the elderly. This in part explains the high prevalence of comorbidities (chronic obstructive pulmonary disease, sleep apnea, cognitive disorders, arthrosis/arthritis, depression, cancer, anemia) in general and of renal failure in particular. (2, 3)

The presence of renal failure in these patients is associated with higher risk for total and cardiovascular mortality, and for hospitalizations due to any reason and to decompensated heart failure. (4-6) This association is independent of age and ventricular function. (4-6)

Braunstein et al. studied a group of U.S. Medicare beneficiaries aged ≥ 65 with CHF. Thirty nine percent of patients had ≥ 5 non-cardiac comorbidities, and only 4% had isolated CHF. (7) One of the most common comorbidities was chronic renal failure. Although patients with ≥ 5 comorbidities comprised 39% of the population, they accounted for 81% of total hospital days. Half of all the hospitalizations were considered potentially preventable. In this cohort, chronic respiratory conditions (RR 2.34; CI 95% 2.27 to 2.41) and renal failure (RR 1.65; IC 95% 1.58 to 1.73) were the variables associated with the greatest relative risks for death. In the study by Acosta et al., 42% of patients with CHF and renal failure had some additional non-cardiac comorbidity.

These data highlight the complexity in the management of patients with CHF in clinical practice, because of the confluence of comorbidities that determine the prognosis independently of the presence and severity of CHF. Some of the reasons that explain why patients with comorbidities more often experience adverse events that result in preventable hospitalizations and worse survival include: 1) the underuse of effective treatments for CHF for safety reasons (like beta-blockers in patients with COPD, or the ACE inhibitors in patients with renal failure), 2) the lack of adherence to complex drug regimens, or the

incapacity to remember them (the average number of drugs prescribed to patients ≥ 65 years of age with a diagnosis of heart failure is 6.8, which represents an average of 10.1 dose per day), 3) inadequate outpatient care, inappropriate social support, and failures in finding and accessing to health care immediately at the recurrence of symptoms, (8) 4) at the same time, patients with multiple comorbidities and polypharmacy are more exposed to drug interactions, 5) finally, the major burden of chronic diseases may decrease the physiologic reserve and expose the carriers to a greater number of acute events.

As Acosta et al. explain, patients with comorbidities in general and with renal failure in particular are underrepresented in the clinical trials that proved the efficacy of several treatments for CHF. (9) Beta-blockers were the most studied drugs in patients with CHF and renal failure, and data from both the post hoc analyses of the CIBIS II (bisoprolol) and MERIT-HF (metoprolol CR/XL) trials, as well as from a small randomized trial (114 patients) with carvedilol in patients with CHF on hemodialysis, show their efficacy and safety in a broad spectrum of patients with renal failure. (10-12) As for inhibitors of the renin-angiotensin-aldosterone system, data are more limited. However, retrospective analysis of the CHARM trial suggests that efficacy and safety of the angiotensin receptor blocker candesartan was not influenced by the presence of moderate renal failure. Data from other observational studies also suggest the efficacy of ACE inhibitors in patients with heart failure and moderate renal failure. (4, 6, 13) After initiation of ACE inhibitors/ARBs, an increase in creatinine may be observed, which implies a more careful monitoring than that for patients with no renal failure. Despite published data in favor of its use, patients with CHF and renal failure are less likely than their counterparts with no renal failure to receive these treatments. (6)

The combination of being older and having multiple chronic pathologies that require treatment represents a poor prognosis for patients, and a major challenge for the physicians in charge of them. It is necessary that research efforts be directed to determine the best strategy for patient management, which should include a multidisciplinary team.

The study by Acosta et al. is a substantial contribution to estimate the magnitude of the problem of comorbidities in CHF in the clinical practice. We still lack data about the population with CHF and preserved

¹ Coronary Care Unit Coordinator at Hospital El Cruce, Florencio Varela, Province of Buenos Aires, Argentina.

systolic function, and its late evolution. It will be necessary to complement it in order to understand the real dimensions of this problem, and to plan interventions that improve the clinical evolution of patients.

BIBLIOGRAPHY

1. Acosta A, Migliori M, Vainstein N, Marino JC, Guglielmo R, Trivi MS et al. Perfil clínico y funcional de los pacientes con insuficiencia cardíaca sistólica y disfunción renal. *Rev Argent Cardiol* 2009; 77:286-92.
2. Krum H, Gilbert RE. Demographics and concomitant disorders in heart failure. *Lancet* 2003; 362:147-58.
3. Lang CC, Mancini DM. Non-cardiac comorbidities in chronic heart failure. *Heart* 2007; 93:665-71.
4. Hillege HL, Nitsch D, Pfeffer MA, Swedberg K, McMurray JJ, Yusuf S, et al; Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) Investigators. Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. *Circulation* 2006; 113:671-8.
5. Fonarow GC, Heywood JT. The confounding issue of comorbid renal insufficiency. *Am J Med* 2006; 119:S17-25.
6. Ezekowitz J, McAlister FA, Humphries KH, Norris CM, Tonelli M, Ghali WA, Knudtson ML; APPROACH Investigators. The association among renal insufficiency, pharmacotherapy, and outcomes in 6,427 patients with heart failure and coronary artery disease. *J Am Coll Cardiol* 2004; 44:1587-92.
7. Braunstein JB, Anderson GF, Gerstenblith G, Weller W, Niefeld M, Herbert R, Wu AW. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. *J Am Coll Cardiol* 2003; 42:1226-33.
8. Masoudi FA, Baillie CA, Wang Y, Bradford WD, Steiner JF, Havranek EP, et al. The complexity and cost of drug regimens of older patients hospitalized with heart failure in the United States, 1998-2001. *Arch Intern Med* 2005;165:2069-76.
9. Coca SG, Krumholz HM, Garg AX, Parikh CR. Underrepresentation of renal disease in randomized controlled trials of cardiovascular disease. *JAMA* 2006; 296:1377-84.
10. Erdmann E, Lechat P, Verkenne P, Wiemann H. Results from post-hoc analyses of the CIBIS II trial: effect of bisoprolol in high-risk patient groups with chronic heart failure. *Eur J Heart Fail* 2001; 3:469-79.
11. Ghali JK, Wikstrand J, Van Veldhuisen DJ, Fagerberg B, Goldstein S, Hjalmarsen A, et al; MERIT-HF Study Group. The influence of renal function on clinical outcome and response to beta-blockade in systolic heart failure: insights from Metoprolol CR/XL Randomized Intervention Trial in Chronic HF (MERIT-HF). *J Card Fail* 2009; 15:310-8.
12. Cice G, Ferrara L, D'Andrea A, D'Isa S, Di Benedetto A, Cittadini A, et al. Carvedilol increases two-year survival in dialysis patients with dilated cardiomyopathy: a prospective, placebo-controlled trial. *J Am Coll Cardiol* 2003; 41:1438-44.
13. Frances CD, Noguchi H, Massie BM, Browner WS, McClellan M. Are we inhibited? Renal insufficiency should not preclude the use of ACE inhibitors for patients with myocardial infarction and depressed left ventricular function. *Arch Intern Med* 2000; 160:2645-50.