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Assessment and Management of Heart Failure in Patients with Chronic Kidney Disease

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Abstract: Heart failure (HF) and chronic kidney disease (CKD) are two pathological conditions with a high prevalence in the general population. When they coexist in the same patient, a strict interplay between them is observed, such that patients affected require a clinical multidisciplinary and personalized management. The diagnosis of HF and CKD relies on signs and symptoms of the patient but several additional tools, such as blood-based biomarkers and imaging techniques, are needed to clarify and discriminate the main characteristics of these diseases. Improved survival due to new recommended drugs in HF has increasingly challenged physicians to manage patients with multiple diseases, especially in case of CKD. However, the safe administration of these drugs in patients with HF and CKD is often challenging. Knowing up to which values of creatinine or renal clearance each drug can be administered is fundamental. With this review we sought to give an insight on this sizable and complex topic, in order to get clearer ideas and a more precise reference about the diagnostic assessment and therapeutic management of HF and CKD.

Keywords: Heart failure, Chronic kidney disease, Biomarkers, Cardio-renal syndrome Guidelines-directed medical therapy.

Introduction

The management of heart failure (HF) has greatly improved during the recent years, but the prognosis remains poor [1]. Moreover, population aging and an increased survival after myocardial infarction are two factors that have changed patients' profiles [2]. HF is often a concurrent condition in elderly patients with many prognosis-relevant comorbidities, such as diabetes mellitus, lung diseases, and vascular diseases. Among these, one of the most frequent is chronic kidney disease (CKD). Furthermore, HF and CKD share the same risk factors such as atherosclerosis, hypertension, diabetes mellitus, obesity, tobacco use, dyslipidemia, negatively affecting the function of both organs. They also have in common the same pathophysiological bidirectional pathways, such as endothelial dysfunction, sympathetic neurohormonal activation, inflammation, and oxidative stress. These processes converge and promote, over time, the dysfunction of both organs [3]. Therefore, the diagnostic and therapeutic management of this subset of patients are particularly challenging, requiring a multidisciplinary and personalized approach to minimize disease progression and maximize efficacy and safety of the therapeutic options.

Epidemiology

Different meta-analyses of randomized controlled studies have shown that 49% of patients with HF suffered from CKD, with eGFR values below 60 mL/min/1.73 m2 [4]. In the Atherosclerosis Risk In Communities (ARIC) study, the incidence of HF was threefold higher in people with an eGFR < 60 mL/min/1.73 m2 compared to those with a preserved kidney function [5]. The Acute Decompensated Heart Failure National Registry (ADHERE) points out that approximately 30% of patients admitted to hospital for acute decompensated HF are affected by acute or chronic kidney disease [6, 7]. The prevalence of CKD was higher in acute HF patients (53%) compared with chronic HF patients (42%). Kidney impairment is a predictor of a poor prognosis in patients with HF and it has a strong

association with worse outcomes [8]. In fact, CKD is related to a higher mortality risk in patient with HF [hazard ratio (HR) 2.34–95% confidence interval (CI) 2.20–2.50] [9].

The cardio-renal syndrome

The cardio-renal syndrome (CRS) represents a disorder of the heart and kidney characterized by the onset of acute or chronic dysfunction in one organ which promote the acute or chronic dysfunction of the other [10]. Several mechanisms are involved in the development of CRS, such as hemodynamic alterations, neurohormonal dysregulation, inflammatory activation, fibrosis, endothelial dysfunction, atherosclerosis, and, above all, arterial stiffness, a pathological alteration of the vascular wall. All the aforementioned conditions trigger a vicious circle with mutual damage leading to the progression of cardiac and kidney disease [11].

Löfman et al. in 2017 showed that in HF with a preserved ejection fraction (HFpEF), CKD was more common and with a better prognosis than HF with a reduced ejection fraction (HFrEF) and HF with a mildly reduced ejection fraction (HFmrEF) [12]. In HFpEF co-morbidity, such as CKD, play a pivotal role, inducing an inflammatory state with microvascular dysfunction potentially leading to both cardiac and renal fibrosis. It has been proposed that HFpEF patients are more susceptible to low blood pressure, being more preload dependent and having more autonomic dysfunction with ventricular and arterial stiffness [12]. The renal hypoperfusion in HF induces the activation of the renin-angiotensin-aldosterone system (RAAS) together with sympathetic nervous system, leading to renal and systemic vasoconstriction, which in turn promotes the secretion of vasopressin. Accordingly, the fluid overload leads to renal interstitial hypertension with necrosis of tubular epithelium, tubular hypertrophy, fibrosis, and permanent tubular injury, increasing central venous pressure and venous return of right ventricle, oxidative stress, the production of proinflammatory cytokines, which exacerbate renal and cardiac remodeling through profibrotic mechanisms, finally causing a worsening of cardiac and kidney functions [12]. This situation leads to the increase of peripheral systemic resistance, arterial stiffness, filling pressures, and the thickening of left ventricle myocardial walls.

Biomarkers

The diagnosis of HF and CKD relies on signs and symptoms, together with cardiac and renal anomalies either structural or functional. Blood biomarkers add further information on the cardiac and kidney damage, given their diagnostic, prognostic, and predictive role. As regard the cardiac evaluation, plasma concentrations of natriuretic peptides such as B type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) are recommended as initial diagnostic test in patients with clinical suspicion of HF to rule out the diagnosis [13, 14]. Natriuretic peptides are mainly synthesized and secreted by myocytes of the left ventricle as a response to the stretch of myocardial walls caused by pressure overload or volume expansion. NT-pro-BNP has a limited diagnostic utility due to high between-person variation related to the influence of several pathophysiological factors on its clearance (hydration status, residual renal function, dialysis regimens), which may hamper the identification of a diagnostic cut-off value in end-stage kidney disease on dialysis [15]. The within-person variability of NT-pro-BNP values is less pronounced, suggesting that a relative-change strategy may improve NT-proBNP diagnostic utility in this population. However, serial NT-proBNP concentrations need to double or halve to confidently exclude change caused by analytic and biologic variations [16]. A correction of NT-pro-BNP values according to age and eGFR may be useful and several studies sought to provide reference values according to the type of HF onset (i.e., acute vs. chronic) and CKD stages, although they are not yet validated in clinical practice [17–19]. The results of these studies are reported in The BNP metabolism is mainly non-renal, mediated by the binding to the natriuretic peptide receptor type C (NPR-C) and through proteolysis by neutral endopeptidases;

thus, its concentration in CKD patients is less affected by eGFR, without the need of a correction of values in patients with CKD stages 1–2 [20]. In asymptomatic HF patients, the rise of BNP blood levels reflects left ventricular overload, predicting a high risk of symptom development. For patients with CKD and HF, a high BNP strongly predicts cardiovascular events and death from all causes.

Moreover, patients with a reduction of BNP after treatment have a better prognosis than those with an increase or stable values of BNP [21].

Given the reduced renal excretion, patients with CKD accumulate toxins, which can cause specific damage to cardiomyocytes. P-cresyl sulfate, a cresol-derived protein bound toxin, and asymmetric dimethylarginine, a product of protein catabolism in cells, are related to cardiovascular outcome and mortality in recent studies and they may contribute to cardiac hypertrophy and endothelial dysfunction in in vitro experiments [22, 23]. Although promising, the role of these toxins in HF management is not sufficiently specified and validated in clinical practice. These and other toxins could explain elevated biomarkers of myocyte damage as eGFR decreases. Myocyte damage biomarkers play an important role in the diagnostic and prognostic evaluation of patients with HF and CKD. The increase of high-sensitive troponin T (HsTnT), the most significant biomarker of myocyte injury, is related with the severity of HF and may correlate with poor prognosis in patients hospitalized with HF [21]. In case of CKD and HF, the cut-off value of all-cause death should be adjusted according to eGFR. HsTnT can predict death in CKD patients without cardiac symptoms and may predict the occurrence of HF. As the eGFR decreases, the prediction accuracy of HsTnT slightly decreases, particularly for CKD stage 5 [24]

In PD water and solute are removed over the perito- neal membrane by dwelling dialysate solution in the peritoneal cavity. Dialysate solution by an osmotic gradient drive peritoneal UF while convective and diffusive forces induce solute removal, including the removal of sodium and potassium [118]. Crystalloid and colloid dialysate solutions are currently available. Crystalloid solutions are dextrose or amino acid based and they induce solute-free water transport across the water channels of peritoneal membrane. Colloid osmosis, induced by a mixture of glucose polymers (maltodextrins) called icodextrin, does not induce free water transport but UF with solutes. Icodextrin allows for more sodium removal compared to an equal UF volume induced with a dextrose-based solution. Moreover, the UF volume is higher than conventional dextrose solutions, although with a lower rate of ultrafiltration at the onset of dialysis but sustained over a longer period Both CAPD and APD regimens have been proposed to treat fluid overload in HF. In patient with significant residual kidney function, as first regimen a single manual night-time icodextrin exchange, which is able to maintain slow and constant UF during long dwells, can be used. If clinically required, PUF can be increased with two exchanges/day using glucose, at concentrations that vary according to the UF obtained, plus a night-time exchange with icodextrin. Alternatively, APD, that uses a machine for exchanges (cycler), can be used up to 3–4 sessions/week using different concentrations of glucose in night-time and icodextrin in daytime. Patients with HF and advanced stage 5 CKD require full dose PD regimens that include CAPD with 3–5 dwell periods/day or daily APD [121].

Conclusions

Many clinical studies have shown that most of drugs indicated as first line treatment by guidelines for HF are effective in improving patient prognosis and they can also be used in patients with mild to moderately impaired kidney function. Many of these studies have mostly excluded patients with advanced chronic kidney failure (eGFR < 20–30 mL/ min/1.73 m2) with less safety per treatment in this group. Therapy for HF in patients with CKD remains difficult,poorly demonstrated, poorly established and standardized, but nevertheless undergoing research. Future studies should address patients with advanced chronic kidney failure and kidney replacement therapy to facilitate their managemen and support the clinician in therapeutic choices.

References

1. Bui AL, Horwich TB, Fonarow GC (2011) Epidemiology and risk profile of heart failure. Nat Rev Cardiol 8:30–41. https:// doi. org/ 10. 1038/ nrcar dio. 2010. 165
2. Triposkiadis F, Giamouzis G, Parissis J, Starling RC, Boudoulas H, Skoularigis J, Butler J, Filippatos G (2016) Reframing the association and significance of co-morbidities in heart failure. Eur J Heart Fail 18:744–758. https:// doi. org/ 10. 1002/ ejhf. 600

3. Damman K, Tang WH, Testani JM, McMurray JJ (2014) Termi-nology and definition of changes renal function in heart failure. Eur Heart J 35:3413–3416. https:// doi. org/ 10. 1093/ eurhe artj/ehu320

4. Damman K, Valente MA, Voors AA, O'Connor CM, van Veldhuisen DJ, Hillege HL (2014) Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. Eur Heart J 35:455–469. https:// doi. org/ 10. 1093/ eurhe artj/ eht386

5. Kottgen A, Russell SD, Loehr LR, Crainiceanu CM, Rosamond WD, Chang PP, Chambless LE, Coresh J (2007) Reduced kidney function as a risk factor for incident heart failure: the athero-sclerosis risk in communities (ARIC) study. J Am Soc Nephrol 18:1307–1315. https:// doi. org/ 10. 1681/ ASN. 20061 01159

6. Heywood JT, Fonarow GC, Costanzo MR, Mathur VS, Wigneswaran JR, Wynne J, Committee ASA Investigators (2007) High prevalence of renal dysfunction and its impact on outcome in 118,465 patients hospitalized with acute decompensated heart failure: a report from the ADHERE database. J Card Fail 13:422–430. https:// doi. org/ 10. 1016/j. cardf ail. 2007. 03. 011

7. Adams KF Jr, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP, Committee ASA et al (2005) Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 149:209–216. https:// doi. org/ 10. 1016/j. ahj. 2004. 08. 005

8. Hillege HL, Nitsch D, Pfeffer MA, Swedberg K, McMurray JJ,Yusuf S, Granger CB, Michelson EL, Ostergren J, Cornel JH et al (2006) Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. Circulation 113:671–678. https:// doi. org/ 10. 1161/ CIRCU LATIO NAHA. 105. 580506

9. Damman K, Testani JM (2015) The kidney in heart failure: an update. Eur Heart J 36:1437–1444. https:// doi. org/ 10. 1093/ eurhe artj/ ehv010

10. Ronco C, Ronco F (2012) Cardio-renal syndromes: a systematic approach for consensus definition and classification. Heart Fail Rev 17:151–160. https:// doi. org/ 10. 1007/ s10741- 010- 9224-0

11. Junho CVC, Trentin-Sonoda M, Panico K, Dos Santos RSN, Abrahao MV, Vernier ICS, Furstenau CR, Carneiro-Ramos MS (2022) Cardiorenal syndrome: long road between kidney and heart. Heart Fail Rev 27:2137–2153. https:// doi. org/ 10. 1007/ s10741- 022- 10218-w

12. Lofman I, Szummer K, Dahlstrom U, Jernberg T, Lund LH (2017) Associations with and prognostic impact of chronic kidney disease in heart failure with preserved, mid-range, and reduced ejection fraction. Eur J Heart Fail 19:1606–1614. https://doi. org/ 10. 1002/ ejhf. 821

13. Moertl D, Berger R, Struck J, Gleiss A, Hammer A, Morgenthaler NG, Bergmann A, Huelsmann M, Pacher R (2009) Comparison of midregional pro-atrial and B-type natriuretic peptides in chronic heart failure: influencing factors, detection of left ventricular systolic dysfunction, and prediction of death. J Am Coll Cardiol 53:1783–1790. https:// doi. org/ 10. 1016/j. jacc. 2009. 01. 057

14. Guaricci AI, Pontone G, Fusini L, De Luca M, Cafarelli FP, Guglielmo M, Baggiano A, Beltrama V, Muscogiuri G, Mushtaq S et al (2017) Additional value of inflammatory biomarkers and carotid artery disease in prediction of significant coronary artery disease as assessed by coronary computed tomography angiog-raphy. Eur Heart J Cardiovasc Imaging 18:1049–1056. https://doi. org/ 10. 1093/ ehjci/ jew173

15. Mahmood U, Johnson DW, Fahim MA (2017) Cardiac biomark-ers in dialysis. AIMS Genet 4:1–20. https:// doi. org/ 10. 3934/genet. 2017.1.1

16. Fahim MA, Hayen A, Horvath AR, Dimeski G, Coburn A, Johnson DW, Hawley CM, Campbell SB, Craig JC (2015) N-terminal pro-B-type natriuretic peptide variability in stable dialysis patients. Clin J Am Soc Nephrol 10:620–629. https://doi. org/ 10. 2215/ CJN. 09060 914

17. Horii M, Matsumoto T, Uemura S, Sugawara Y, Takitsume A, Ueda T, Nakagawa H, Nishida T, Soeda T, Okayama S et al (2013) Prognostic value of B-type natriuretic peptide and its amino-terminal proBNP fragment for cardiovascular events with stratification by renal function. J Cardiol 61:410–416. https:// doi. org/ 10. 1016/j. jjcc. 2013. 01. 015

18. Zelenak C, Chavanon ML, Tahirovic E, Trippel TD, Tscholl V, Stroux A, Veskovic J, Apostolovic S, Obradovic D, Zdravkovic M et al (2019) Early NT-proBNP and MR-proANP associated with QoL 1 year after acutely decompensated heart failure: secondary analysis from the MOLITOR trial. Biomark Med 13:1493–1507. https:// doi. org/ 10. 2217/ bmm- 2019- 0083

19. Schaub JA, Coca SG, Moledina DG, Gentry M, Testani JM, Parikh CR (2015) Amino-terminal pro-B-type natriuretic pep-tide for diagnosis and prognosis in patients with renal dysfunc-tion: a systematic review and meta-analysis. JACC Heart Fail 3:977–989. https:// doi. org/ 10. 1016/j. jchf. 2015. 07. 014

20. Sato Y (2013) Diagnostic and prognostic property of NT-proBNP in patients with renal dysfunction. J Cardiol 61:446–447. https://doi. org/ 10. 1016/j. jjcc. 2013. 01. 013

21. Hollenberg SM, Warner Stevenson L, Ahmad T, Amin VJ, Bozkurt B, Butler J, Davis LL, Drazner MH, Kirkpatrick JN, Peterson PN et al (2019) 2019 ACC expert consensus decision pathway on risk assessment, management, and clinical trajectory of patients hospitalized with heart failure: a report of the Ameri-can College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 74:1966–2011. https:// doi. org/ 10. 1016/j. jacc. 2019. 08. 001

22. Glorieux G, Vanholder R, Van Biesen W, Pletinck A, Schepers E, Neirynck N, Speeckaert M, De Bacquer D, Verbeke F (2021) Free p-cresyl sulfate shows the highest association with cardiovascular outcome in chronic kidney disease. Nephrol Dial Transplant 36:998–1005. https:// doi. org/ 10. 1093/ ndt/ gfab0 04

23. Sapa H, Gutierrez OM, Shlipak MG, Katz R, Ix JH, Sarnak MJ, Cushman M, Rhee EP, Kimmel PL, Vasan RS et al (2022) Asso-ciation of uremic solutes with cardiovascular death in diabetic kidney disease. Am J Kidney Dis 80:502–512.e501. https:// doi. org/ 10. 1053/j. ajkd. 2022. 02. 016

24. Sun J, Axelsson J, Machowska A, Heimburger O, Barany P, Lindholm B, Lindstrom K, Stenvinkel P, Qureshi AR (2016) Biomarkers of cardiovascular disease and mortality risk in patients with advanced CKD. Clin J Am Soc Nephrol 11:1163–1172. https:// doi. org/ 10. 2215/ CJN. 10441 015