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Review

Worsening Renal Function in Elderly Patients with Heart Failure and Chronic Kidney Disease: An Update

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REZUMAT

Agravarea funcției renale la pacienții vârstnici cu insuficiență cardiacă și boală cronică de rinichi: update

Boala cronică de rinichi (BCR) este factor de risc independent și factor agravant pentru afectarea cardiacă. Insuficiența cardiacă decompensată agravează BCR, determinând o evoluție defavorabilă și o mortalitate crescută. Dacă cele două patologii apar la pacientul vârstnic, prognosticul este și mai grav. Rinichiul vârstnic este vulnerabil la declinul funcțional, atât prin scăderea fiziologică a ratei filtrării glomerulare, cât și prin asocierea de morbidități multiple (nefropatie diabetică sau hipertensivă, nefrotoxicitate medicamentoasă). Agravarea funcției renale este definită ca și creșterea creatininei serice cu ≥ 0,3 mg/dL și corespunde stadiului Risk din clasificarea RIFLE a insificienței renale acute. Deteriorarea funcției renale are un prognostic rezervat în ambele tipuri de insuficiență cardiacă - acută și cronică.

Cuvinte cheie: insuficiență cardiacă, boală cronică de rinichi, agravarea funcției renale

ABSTRACT

Chronic kidney disease (CKD) is both an independent risk factor and an aggravating factor for the cardiovascular disease. Decompensated heart failure worsens CKD with adverse outcome and higher mortality. If the two diseases occur in elderly patients the prognosis is even more serious. Kidney function in the elderly is altered both physiologically and through the multiple morbidities (diabetic or hypertensive nephropathy, drug nephrotoxicity). Worsening renal function (WRF) is defined as serum creatinine increase ≥ 0.3 mg/dL.WRF has a poor prognosis in acute and in chronic heart failure.

Key words: heart failure, CKD, worsening renal function

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INTRODUCTION

Chronic kidney disease (CKD) is defined as either kidney damage or eGFR (estimated glomerular filtration rate) < 60 mL/min/1.73 m^2 for three or more months [1]. Elderly patients have often an impaired basal renal function due to intrinsic renal disease or to a physiological decrease in the number of functional nephrons [2]. Half of adults over the age of 70 years have eGFR < 60 mL/min/1.73 m^2 [3]. CKD occurs in about 4.5% of the general population and 50% in patients with chronic or acute heart failure (HF) [4]. Commonly, CKD can be associated with-chronic heart failure in elderly patients [2].

Comorbidities in heart failure patients

In an analysis of European Heart Failure Pilot survey the authors high lighted the most commonly co-morbidities in heart failure patients: CKD (41%), anemia (29%), diabetes (29%), followed by COPD (chronic obstructive pulmonary disease), stroke, sleep apnea, hypothyroidism, hyperthyroidism [5]. Another meta-analysis which totaled overone million patients with heart failure has shown a CKD prevalence of 53% in acute heart failure and 42% in chronic heart failure [2]. Mortality rates in these patients after a mean follow-up of 681±704 days were 16% for patients with CKD and 11% to those without CKD [2].

Worsening renal function

Worsening renal function (WRF) is defined as serum creatinine increase ≥ 0.3 mg/dL [4]. WRF aggravates the prognosis and increases mortality in both in patients and out patients [4]. Increased serum creatinine is called pseudo-WRF if the condition of the patient remains stable or improves [4]. In acute heart failure, a slight increase in serum creatinine may be accepted if clinical condition does not deteriorate [4]. WRF has a poor prognosis in both acute heart failure (which is associated with decreased systolic blood pressure) and chronic heart failure, except when it is secondary to increased dose of ACE inhibitor [2].

The pathophysiological mechanisms of heart-kidney determination are highly complex and still poorly known, particularly in acute heart failure [4,6,7]. They involve renal mechanisms (loss of functional nephrons, renal fibrosis, acute tubulointerstitial injury, decreased GFR, decreased renal blood flow, albuminuria, renal congestion, retention of Na/water), cardiac mechanisms (reduced cardiac output, increased CVP – central venous pressure, increase wall stress, myocardial injury, myocardial fibrosis), and modulators factors (RAAS – renin–angiotensin–aldosterone system activation, SNS –sympathetic nervous system activation, endothelial dysfunction, anemia, inflammation) [4].

Acute heart failure increases congestion and decreases renal blood flow, with reduced oxygen delivery and increased albuminuria [4]. The oxygen consumption of the functional nephrons is increased because sodium reabsorption is done with high energy consumption [4]. The two pathophysiological mechanisms are leading to renal tubular injury [4]. NT-proBNP (N-terminal of the prohormone brain natriuretic peptide) and increased BUN (blood urea nitrogen)/creatinine ratio, the major markers of organ dysfunction, are identifying renal dysfunction induced HF [4,8,9]. NT-proBNP reduction > 30% is indicative of survival after hospitalization in patients with acutely decompensated heart failure, more than WRF [10].

In elderly patients, acute decompensated heart failure secondary to venous congestion has immediate consequence on WRF [2]. Any degree of CKD increases the risk of death in patients with heart failure, by WRF [2]. Comorbidities as hypertension, diabetes, anemia, or high doses of diuretics are also contributing to WRF in acute decompensated heart failure [2].

Key management in heart failure with CKD

ESC (European Society of Cardiology) guidelines for the treatment of heart failure recommend an ACE (angiotensin-converting enzyme) inhibitor, in addition to a beta-blocker for all patients with an EF (ejection fraction) ≤ 40% [11]. For the patients with NYHA class II-IV heart failure and EF ≤ 35%, with persisting symptoms despite the previous medication, ESC guidelines recommend an MRA (mineralocorticoid receptor antagonists) [11]. Some authors showed that heart failure treatment (ACEi/ARB (angiotensin receptor blocker), beta-blocker, MRA, diuretic, digoxin, ivabradine, H-ISDN – Hydralazine-IsosorbideDinitrate, intracardiac device) in patients with stage 3-5 CKD produced more a reduction in hospitalization period than a decreased mortality rate [12]. Other authors reported a 2 to 3-fold increase in life expectancy in case of combination of ACE inhibitor, beta-blocker and MRA [13]. In clinical practice doses may not be the same level as in the trials, but must be titrated as up as possible [13]. Clinical Practice guidelines recommend treatment with maximally tolerated dose of ACEi and a lipophilic beta-blocker for all CKD patients staged 3b or higher with diabetes and heart failure [14]. The pharmacokinetic properties of ACEi, the renal elimination and the T1/2 determine the dose adjustments of ACEi/ARB at one-half dosage to one-eight dosage or even the administration only in the dialysis days [12]. The recommended beta-blockers in heart failure patient with CKD are carvedilol (T1/2 = 6h, fecal elimination and no dose adjustment if systolic blood pressure are above 100 mmHg), metoprolol (T1/2= 3.5-9 h, lower dose in reduced eGFR), nebivolol (T1/2= 10-50h, elimination by 48% fecal and 38% renal, one-half dose in reduced eGFR) [11]. MRA is contraindicated in severe renal failure [12].

WRF ≥ 0.5 ng/dL is a strong and independent predictor of death [15]. ACE inhibitors decreasese GFR in the early started treatments. A similar effect, but

with less intensity, have the beta-blockers [4]. The beneficial effect of these drugs is maintained despite a slight increase in serum creatinine, but need repeated assessment of the renal function and serum potassium levels [4]. The adjusted doses of ACE inhibitors /ARB and beta-blockers according to NT-proBNP were not associated with severe WRF [15]. Renal function should be monitored both during hospitalization and in the first three months after hospitalization [16].

WRF occurs frequently in patients treated with high dose of loop diuretics (>160 mg/day Furosemide) an spironolactone [15].

Decongestive therapy and RAAS inhibitors reduce NT-proBNP. A more aggressive therapy in case of insufficient NT-proBNP reduction is accepted, with the risk of WRF [4].

Studies have shown that in chronic heart failure, loop diuretics reduce the urinary markers of renal impairment (NAG – N-acetyl-beta-D-glucosaminidase, KIM-1 – Kidney Injury Molecule-1) [4]. In acute heart failure loop diuretics improves albuminuria [4]. DOSE-trial investigators studied the doses and different regimens of administration of loop diuretics in acute heart failure [4,17]. Although the results were similar at discharge, high dose loop diuretics were associated with venous congestion reduction, but with higher incidence of WRF [4,17].

In UNLOAD and RAPID-CHF trials, the investigators showed that ultrafiltration reduced the venous congestion and the renal venous pressure, but not improved the kidney function compared to loop diuretics [4,18,19].

WRF secondary to haemoconcentration, diuretic therapy, complete decongestion, low blood pressure or to specific heart failure initiating therapy (ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonist) has a better prognosis than unprovoked WRF [2].

Digoxin need to be administrated in very low doses (0.125 mg every other day in stage 3 CKD) or even less frequently in advanced stage of CKD [20]. Dietary salt restriction, management of hyperphosphatemia, mineral bone disorders and anemia are another key of the treatment [20]. In patients with the two comorbidities, heart failure and CKD, any rising of dose medication or changing the clinical status should be followed by monitoring the eGFR and serum potassium level [21].

CONCLUSIONS

In the elderly chronic kidney disease and heart failure often coexists. WRF has a poor prognosis in both acute and chronic heart failure. Knowledge of pathophysiological mechanisms and side effects of cardiac medication could prevent or ameliorate WRF.

REFERENCES

1. Rosenberg M. Overview of the management of chronic kidney disease in adults. UpToDate. 2015; http://www.uptodate.com/contents/overview-of-the-management-of-chronic-kidney-disease-in-adults.com; accessed November 2015.
2. Damman K, Valente MA, Voors AA, O'Connor CM, van Veldhuisen DJ, Hillege HL. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. Eur Heart J. 2014; 35(7):455-469.
3. Rule AD, Glassock RJ. The aging kidney. UpToDate. 2015; http://www.uptodate.com/contents/the-aging-kidney; accessed November 2015.
4. Damman K, Testani JM. The kidney in heart failure: an updateEur Heart J. 2015; 36(23):1437-1444.
5. vanDeursen VM, Urso R, Laroche C, Damman K, Dahlström U, Tavazzi L, Maggioni AP, Voors AA. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. Eur J Heart Fail. 2014; 16(1):103-111.
6. Di Lullo L, HouseA, Gorini A, Santoboni A, Russo D, Ronco C. Chronic kidney disease and cardiovascular complications. Heart Fail Rev. 2015; 20(3):259-272.
7. Bălăceanu A, Diaconu C, David C, Niculae A, Peride I, Aron G. Vascular calcifications, major risk factor for cardiovascular events in chronic kidney disease: an update on the pathophysiological process. Medicina Modernă. 2014; 21(2):116-119.
8. Nechita AM, Rădulescu D, Peride I, Niculae A, Sinescu DR, Checheriță IA, Ciocâlteu A. Cardiac biomarker NTproBNP in chronic kidney disease – a brief review. Medicina Modernă. 2015; 22(2):136-139.
9. Nechita AM, Rădulescu D, Peride I, Niculae A, Bratu O, Ferechide D, Ciocâlteu A, Checheriță IA, Mischianu D. Determining factors of diuresis in chronic kidney disease patients initiating hemodialysis. J Med Life. 2015; 8(3):371-377.
10. Salah K, Kok WE, Eurlings LW, Bettencourt P, Pimenta JM, Metra M, Verdiani V, Tijssen JG, Pinto YM. Competing risk of cardiac status and renal function during hospitalization for acute decompensated heart failure. JACC Heart Fail.2015, 3(10):751-761.
11. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Køber L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Rønnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A; ESC Committee for Practice Guidelines. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012; 33(14):1787-1847.
12. Damman K, Tang WH, Felker GM,Lassus J, Zannad F, Krum H, McMurray JJ. Current evidence on treatment of patients with chronic systolic heart failure and renal insufficiency. J Am CollCardiol. 2014; 63(9):853-871.
13. Cole GD, Patel SJ, Zaman N, Barron AJ, Raphael CE, Mayet J, Francis DP. "Triple Therapy" of heart failure with angiotensin-converting enzyme inhibitor, beta-blocker, and aldosterone antagonist may triple survival time: shouldn't we tell patients? JACC Heart Fail.2014; 2(5):545-548.
14. Bilo HJ et al. Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR<45 mL/min). Nephrol Dial Transplant. 2015; 30(Suppl 2): ii1-ii142.
15. Maeder MT, Rickli H, Pfisterer ME, Muzzarelli S, Ammann P, Fehr T, Hack D, Weilenmann D, Dieterle T, Kiencke S, Estlinbaum W,

Brunner-La Rocca HP; TIME-CHF Investigators. Incidence, clinical predictors, and prognostic impact of worsening renal function in elderly patients with chronic heart failure on intensive medical therapy. Am Heart J. 2012; 163(3):407-414, 414.e1.

16. SheerinNJ, Newton PJ, Macdonald PS, Leung DY, Sibbritt D, Spicer ST, Johnson K, Krum H, Davidson PM.Worsening renal function in heart failure: the need for a consensus definition. Int J Cardiol. 2014;174(3):484-491.
17. Felker GM, Lee KL, Bull DA, Redfield MM, Stevenson LW, Goldsmith SR, LeWinter MM, Deswal A, Rouleau JL, Ofili EO, Anstrom KJ, Hernandez AF, McNulty SE, Velazquez EJ, Kfoury AG, Chen HH, Givertz MM, Semigran MJ, Bart BA, Mascette AM, Braunwald E, O'Connor CM. Diuretic strategies in patients with acute decompensated heart failure. N Engl J Med. 2011;364(9):797-805.
18. Costanzo MR, Guglin ME, Saltzberg MT, Jessup ML, Bart BA, Teerlink JR, Jaski BE, Fang JC, Feller ED, Haas GJ, Anderson AS, Schollmeyer MP, Sobotka PA; UNLOAD Trial Investigators. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. J Am CollCardiol. 2007;49(6): 675-683.
19. Bart BA, Boyle A, Bank AJ, Anand I, Olivari MT, Kraemer M, Mackedanz S, Sobotka PA, Schollmeyer M, Goldsmith SR. Ultrafiltration versus usual care for hospitalized patients with heart failure: the Relief for Acutely Fluid-Overloaded Patients with Decompensated Congestive Heart Failure (RAPID-CHF) trial. J Am CollCardiol. 2005;46(11):2043-2046.
20. Segall L, Nistor I, Covic A. Heart failure in patients with chronic kidney disease: a systematic integrative review. Biomed Res Int. 2014; 2014:937398.
21. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Managementof Chronic Kidney Disease;www.kdigo.org/ clinical_ practice_guidelines; accessed November 2015.