Horizon | Journal of Humanity and Artificial Intelligence

ASPECTS OF CLINICAL PATHOGENETIC EARLY DIAGNOSIS OF CHRONIC HEART FAILURE IN CHRONIC KIDNEY DISEASE

Nadirova Yulduz Isomovna, Jabbarov Ozimboy Otaxonovich, Mirzayeva Gulchehra Payzullayevna, Buvamuhamedova Nasiba Toxirovna
Tashkent medical academy

Abstract

The most important advancements in the Cardiorenal syndrome (CRS) are its definition and subsequent classifications. When the predominant pathology and pathophysiology is the heart, i.e. chronic heart failure (CHF), and where any renal impairment (RI) subsequent to this is secondary, the classification is type 2 CRS. There are unique differences in the pathophysiology and progression of individual subclasses. It is important to understand the evolution of CHF and consequences of subsequent RI as they are becoming increasingly prevalent, aggravate morbidity and mortality and limit many therapeutic options. In this paper we discuss the significance of the type 2 CRS patients in the context of the thematic series.

Keywords: Congestive Heart Failure, Cardiorenal Syndrome, Indigenous Australians, Renal Failure, Treatment, Cardiorenal Syndrome

INTRODUCTION

The cardiorenal syndrome (CRS) and many aspects in the understanding of this disease have been advanced enormously over the last decade. The association between renal failure and accelerated atherosclerosis was described by, Lindner et al, in 1974 [1]. In the latter years it was noticed that the umbrella term CRS was not sufficient to explain all the pathophysiological findings, the pathology in the organs, diagnosis and even management [2]. The combined group efforts and international consensus have consolidated CRS into five accepted sub-classes [3, 4]. Much of the future impetus will be to understand each of the individual subclasses better. The type 2 CRS is perhaps the most established for much of the early interest. Chronic Heart Failure (CHF) eventually causes renal impairment (RI) in nearly all cases, however, there are many other factors that can also contribute. These factors are critical in the sub classifications which are based on 2 principles: firstly, the organ predominately involved, thus the direction of the interaction; secondly, the chronology, predominately acute or chronic. The severity of involvement has not been factored.

CHF in isolation can inflict tremendous cost to health systems, approximately 2% where 60% of the cost is for hospitalizations [5-7]. It is also the most common cause of

hospitalization over 65 years in the US and 5% of internal medical admissions in Europe. Readmissions are high between a third to one half in 6 months. Mortality is around 13% within 12 weeks of discharge in European cohorts [8-10]. In hospital mortality is between 4-7% and 5 year

mortality approaching 60% [8, 11]. The incidence of 0.2-0.3% rises greatly with age to as high as 10 fold in those over 80 years of age [12]. Prevalence, from Rotterdam study, similarly shows rises from less than 1% between 55 and 64 years to 13% between 75 and 84 years [13]. With rapid aging, the temporal trend shows a steep increase in the developed world. This will also affect the quality of life of patients and their families [3]. Without factoring cardiac diseases, renal diseases also contribute to excess morbidity and mortality [14]. Similarly, cardiorenal interactions are worse than the individual organ pathologies. Here the severity of disease in either organ will naturally contribute to greater overall risks [15]. This review is focused on exploring the role of the kidney in CHF, particularly in the real world setting, or outside the controls of the randomized control trials. As there have been numerous publications on specifics and variants of CRS, we aim to maintain a context of the editorial theme [2, 3, 16]. We discuss the interaction between CHF and RI, now commonly known as the type 2 CRS.

Epidemiology

There are sufficient studies from which results have been pooled to get an overview of the CRS. We know similarly that in isolation, CHF averages a 50% 5-year mortality and End Stage Renal Failure (ESRF) similarly [17, 18]. Similarly, RI is a risk factor for CHF [19, 20]. We are now sub-classifying the intermediate grades, where as CHF becomes more severe and the risk of renal impairment also becomes greater. As we can see from the above definition, the working group made clarifications to better understand broader possibilities. There are very few studies, however that have looked at this longitudinally.

Pathophysiology

The leading cause of CHF, excluding RI, includes ischemic heart diseases and myocardial infarction, diabetes mellitus (DM), the metabolic syndrome and hypertension. Hypercholesterolemia, cigarette smoking, family history and race similarly predispose or cause CHF through secondary means [23]. CHF evolves due a single hit, such as myocardial infarction or a cumulative process of multiple minor effects. Often one confounding entity is poorly controlled and causes significant system stress. When there are common processes, the reason for one organ being affected earlier or greater is unknown, and could perhaps relate to the greater stress on the myocardial cell compared to the others e.g. nephron. Thus, it would be fair to assume, that in theory, that the kidneys are unlikely to be normal to start with. In addition to the identical chronological association between myocyte, nephron and causative comorbidity, there is immediate stress on the kidney through pathophysiological connections when CHF develops.

The kidneys receive 25% of blood flow, where the majority goes to the cortex, which also has the greatest neural innervations to regulate changes acutely. The medulla receives only 10% of the blood supply. The renal microvascular bed however is continuous throughout. Thus, disease in any glomeruli could have implications when placed under supraphysiological stress from SNS or RAAS and matched with early disease in vascular endothelium and nitric oxide systems. Thus, when considering the total glomerular filtration rate (GFR), it is the sum of the contribution of single-nephron GFR (SNGFR). RBF and regulators of transglomerular pressures are among the most important contributors for GFR.

$SNGFR = kf\_x\ \Delta P$.

(kf = coefficient of filtration ΔP = pressure gradient)

Compensation to ensure adequate GFR includes increased renal blood flow (afferent arteriolar vasodilatation), filtration pressure (via efferentarteriolar vasoconstriction) and glomerular hypertrophy, and hyperfiltration (leads to scarring). CHF effects on the kidney become a problem when single nephron filtration fraction (SNFF) and SNGFR are functioning at

reasonable capacity [24].

Diagnostics

The ability to identify cardiovascular decompensation and subsequent renal injury early and accurately are the most important diagnostic tools. Unfortunately, we have still not identified which of these tools will answer the call with accuracy, consistency and cost effectiveness. A glance of the area and promising tools are discussed.

Cardiovascular Diagnostics

Accurate cardiovascular diagnostics has never been an issue since the advent of advanced tissue imaging and invasive coronary catheterization. For clients in more remote parts availability can be a factor. There are also more novel techniques utilizing Doppler, speckle tracking and cardiac MRI to provide information that correlates to earlier changes in the myocardium. While this is a more preventive aspect for CHF, it is nonetheless a beneficial advancement in the area that will spill over for the CRS. What has been more difficult however is determining precisely when patients are at greatest risk of decompensation, impairing renal blood flow and aggravating RF. Invasive device-based diagnostics, from implantable cardioverter defibrillators (ICDs) are available, however, with many technical issues when applied for daily clinical use [25].

Renal Diagnostics

We published a review on the diagnostics in the CRS in 2012, and since that time there have been some important changes. Conventional biomarkers such as urea, and serum creatinine (SCr) remain the main stay. In all cases blood would be analyzed and an estimated GFR (eGFR) is provided. The limitations and consequences with various permutations in the CRS have been previously discussed [24]. The main gap is its failure to provide temporal information for injury or function in two critical situations, firstly, with the commencement of neprotoxic pharmacotherapy, and secondly, the inability of SCr to provide an accurate assessment of function in the acute settings. Cystatin-C (Cys-c), a low molecular weight (13-kDa), an endogenous proteinase inhibitor has a number of features as a reliable marker for injury, RI and eGFR. It originates from any nucleated cell, thus its production and release is constant regardless of age, race, sex, body mass, critical illness. Its levels rise before SCr and it is freely filtered by the glomerulus and completely reabsorbed by the proximal tubule [15]. In 823 CHF patients undergoing coronary angiography, Cys-C based eGFR improved major adverse cardiovascular event prediction independently to SCr and BNP, especially with eGFR $\geq$60 mL/min per 1.73 m^2 ($P<0.01$)

Optimizing CHF Care and Therapeutics

If we are going to focus entirely on delivering novel therapies in established type 2 CRS, we have invariably shifted the risk profile upward. It will be a debate as to when actual type 2 CRS develops, particularly in those with comorbidities that affect multiple organs, thus graying the boundaries on what is truly a prevention. It may also seem unclear as to what additional treatments need to be provided when the pathophysiological principles for treatment including RAAS and SNS blockade in conjunction with good control of comorbidity and risk factors are the same throughout. However, this is not exactly the case. Firstly, the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) study data from 48, 612 patients provided two hundred fifty-nine patients participating in US hospitals with process-of-care improvement tools, which included evidence-based best-practice algorithms and customizable admission and discharge sets. Participation in the study was associated with increase in evidence based prescribtion, shorter hospitalizations and in hospital mortality, and use of process-of-care improvement tools and preprinted admission order sets further improved benefits [5]. Ensuring other factors like staffing and consistency in the distribution of services can also

impact outcomes by ensuring that management for patients is always optimal [7]. The importance of OPTIMIZE-HF for the type 2 CRS was highlighted by Ezekovitz *et al*. who followed 6247 patients with CHF with angiographically proven coronary artery disease for 12 months. RI is common, greater in those with more advanced coronary disease, less likely to be prescribed prognostic therapies but achieve better outcomes when they are. Prognostic therapies seem to be prescribed contarary to CRS severity. In 7,487 patients in SOLVD, 6-17.5% were undertreated due to perceived contraindications where only 11 (0.15%) had azotemia and the average increase in SCr was 0.02 mg/dl [8]. In the HOPE study, hyperkalaemia (< 6.5mmol/l) did not increase cardiac risk but hypokalaemia (<3.5) did [9]. This study and others have raised the issues of inadequate therapies, with subtherapeutic dosing particularly due to few randomized control trial guides to follow and the fear of aggravating RI [15]. This problem can be particularly severe for the elderly where CHF (both systolic and diastolic) and, RI are more prevalent, the severity of both diseases seems to be parallel, and are among the most likely diseases to be undertreated [20, 21].

Conclusion

The classification of secondary RI following established CHF as the type 2 CRS is a much welcomed recent advancement. It is now very clear that there are established cardiorenal links, which requires greater accountability from those only treating the heart. It is also likely that this may evolve into a larger cardiorenalmetabolic axis question. It is, however unfortunate, that many other aspects of the science are not available. There are gaps in: a) epidemiological understanding of the temporal causality; b) pathophysiological understanding of differentials in risk and therapeutic benefits, greater specifics on hemodynamic and cardiac neurohormal factors on nephron filtration, compensation, feedback and risk of fibrosis, and the reverse when RI has developed; c) diagnostics to better predict risk either individually or as a panel which will complement clinical practice with cost-effectiveness; and d) a better and broader understanding of how to safely institute mainstay therapies, when to consider a wider therapeutic paradigm and when to utilize invasive therapeutics, which can be factored into generic CHF guidelines. How we factor research studies to answer these questions are going to be equally challenging. The platform for clinical trials may require a large cohort, but may not receive Industry funding, to answer these questions. What advancement in CRS and the Type 2 CRS is teaching us is that we have the capacity to understand risk better, but are lacking in the tools to routinely diagnose it and execute management better.

REFERENCES

1. Lindner A., Charra B., Sherrard D.J., Scribner B.H. Accelerated atherosclerosis in prolonged maintenance hemodialysis. N. Engl. J. Med. 1974;290:697–701.
2. Жаббаров, А. А., Бувамухамедова, Н. Т., & Мирзаева, Г. Ф. (2021). ОЦЕНКА ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ ПЕЧЕНИ У БОЛЬНЫХ С ИБС НА ФОНЕ БАЗИСНОЙ ТЕРАПИИ В СОЧЕТАНИИ ЭКСТРАКТА РАСТОРОПШИ. *Интернаука*, (4-1), 34-36.
3. Buvamukhamedova, N. T., Jabbarov, O. O., Mirzayeva, G. F., & Madazimova, D. K. (2021). PROSPECTS OF RIVAROXABAN USE IN THE TREATMENT OF PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE. *Oriental renaissance: Innovative, educational, natural and social sciences*, *1*(11), 496-502.

4. Бувамухамедова, Н., Жаббаров, О., Мирзаева, Г., & Рахматов, А. (2022). Перспективы Применения Ривароксабана В Лечении Пациентов С Хронической Ишемической Болезнью Сердца.
5. Мирзаева, Г. П., Жаббаров, О. О., Аликулов, И. Т., Бувамухамедова, Н. Т., & Рахматов, А. М. (2022). Особенности течения подагрического поражения почек у больных с ожирением.
6. Parpibaeva, D. A., Buvamukhamedova, N. T., Ergashev, N. S., Salimova, N. D., & Salaeva, M. S. (2023). Optimization of Functional State of the Liver in Patients with Chd on the Background of Rosuvastatin Intake. *Scholastic: Journal of Natural and Medical Education*, *2*(4), 8-12.
7. Mirzaeva, G. P., Jabbarov, O. O., & Buvamuxamedova, N. T. (2022). FEATURES OF THE COURSE OF GOUTY KIDNEY DISEASE IN PATIENTS WITH OBESITY. *Eurasian Journal of Medical and Natural Sciences*, *2*(13), 159-161.
8. Nazarova, N. O. K., Jabbarov, A. A., Madazimova, D. H., Mirzayeva, G. P., & Buvamuhamedova, N. T. (2021). DECREASED GENE TGF-B1 ARE ASSOCIATED WITH RENAL DAMAGE IN FEMALE PATIENTS WITH LYUPUS NEPHRITIS. *Oriental renaissance: Innovative, educational, natural and social sciences*, *1*(11), 1200-1203.
9. Ayupovna, P. D., Saidabdullayevna, S. M., Djurabaevna, S. N., Shermuxamat o'g'li, E. N., & Taxirovna, B. N. (2023). FENOFIBRATE IN THE COMPLEX TREATMENT OF COMPLICATIONS OF TYPE 2 DIABETIC RETINOPATHY. *Spectrum Journal of Innovation, Reforms and Development*, *15*, 1-8.
10. Mirzayeva, G. P., Jabbarov, O. O., Umarova, Z. F., Tursunova, L. D., & Rahmatov, A. M. (2023). Assessment of Efficacy and Optimization of Antiplatelet Therapy in Patients with Ischemic Heart Disease. *Web of Synergy: International Interdisciplinary Research Journal*, *2*(3), 183-186.
11. Jumanazarov, S., Jabbarov, O., Umarova, Z., Tursunova, L., & Mirzayeva, G. (2022). Factors affecting platelet hemostasis and resistance to curantil in patients with chronic kidney disease.
12. Холов, Х. А., Тешаев, О. Р., Бобошарипов, Ф. Г., Амонуллаев, А. Х., & Надирова, Ю. И. (2023). ОСТРЫЙ ПАНКРЕАТИТ-КАК НЕРЕШЕННАЯ ПРОБЛЕМА МЕДИЦИНЫ. *Академические исследования в современной науке*, *2*(8), 192-206.
13. Бобошарипов, Ф. Г., Холов, Х. А., Тешаев, О. Р., Алимов, С. У., & Надирова, Ю. И. (2023, March). ОСЛОЖНЕНИЕ ОСТРОГО ХОЛЕЦИСТИТА У БОЛЬНЫХ ПЕРЕНЯВШИСЬ COVID-19. In *Международная конференция академических наук* (Vol. 2, No. 3, pp. 41-48).
14. Бобошарипов, Ф. Г., Холов, Х. А., Тешаев, О. Р., Алимов, С. У., & Надирова, Ю. И. (2023). КОМОРБИДНОЕ ТЕЧЕНИЕ ОСТРОГО ХОЛЕЦИСТИТА У БОЛЬНЫХ COVID-19. *Models and methods in modern science*, *2*(4), 51-58.
15. Xodjanova, S. I., Boqiyeva, D. R., Jabbarov, A. A., Umarova, Z. F., Kenjayev, M. L., Saydaliyev, R. S., ... & Nadirova, Y. I. (2023). SURUNKALI YURAK YETISHMOVICHILIGI MAVJUD BEMORLARDA BUYRAK DISFUNKSIYASINING KASALLIK KECHISHIGA TA'SIRI. *Евразийский журнал медицинских и естественных наук*, *3*(1 Part 2), 139-144.
16. Надирова, Ю. И. (2023). ОЦЕНКА ЭФФЕКТИВНОСТИ ПРИ ПРИМЕНЕНИЕ ЮПЕРИО И ГЛИФЛОЗИНЫ У БОЛЬНЫХ ХСН.
17. Надирова Ю. и др. ОПТИМИЗАЦИЯ КОМБИНИРОВАННОЙ ТЕРАПИИ ПРИ БОЛЕЗНИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ БЛОКАТОРОМ КАЛЬЦИЕВЫХ

КАНАЛОВ И ИНГИБИТОРОМ АПФ //Solution of social problems in management and economy. – 2023. – Т. 2. – №. 2. – С. 181-186.

18. Teshaev, O. R., Rakhmonova, G. E., Jumaev, N. A., & Babadjanov, A. B. (2020). A REVIEW OF SPREADING WAYS, FEATURES OF DIAGNOSIS AND TREATMENT OF CORONAVIRUS INFECTION. *Central Asian Journal of Medicine*, *2020*(3), 119-134.
19. Umarova, Z. F., Jabbarov, O. O., Saydaliyev, R. S., Jumanazarov, S. B., & Radjapov, A. B. (2023). DIASTOLIC DYSFUNCTION IN PATIENTS WITH CORONARY ARTERY DISEASE LATE AFTER CORONARY STENTING. *Theoretical aspects in the formation of pedagogical sciences*, *2*(7), 161-164.
20. Абдунабиев, Х. А., Насриддинова, Н. Н., Максудова, М. Х., & Надирова, Ю. И. (2020). ЭФФЕКТИВНОСТЬ САКУБИТРИЛ/ВАЛСАРТАНА У БОЛЬНЫХ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ, ОСЛОЖНЕННОЙ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ. *Студенческий вестник*, (3-2), 64-65.
21. Холов, Х. А., Бобошарипов, Ф. Г., & Надирова, Ю. И. К. (2016). Оптимизация диагностики острого панкреатита. *Биология и интегративная медицина*, (6), 150-159.
22. Бобошарипов, Ф. Г., Холов, Х. А., Тешаев, О. Р., & Надирова, Ю. И. (2023). ПОСТБАРИАТРИЧЕСКАЯ ГИПОГЛИКЕМИЯ И ГИПОТОНИЯ. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *21*(5), 105-113.
23. Надирова, Ю. И., Бобошарипов, Ф. Г., Кодирова, Ш. А., & Мирзаева, Г. П. (2023). ОСТЕОПОРОЗ ПРИ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *21*(5), 89-96.
24. Надирова, Ю. И. (2023). ФАКТОРЫ РИСКА СНИЖЕНИЯ ПРОЧНОСТИ КОСТИ И ПЕРЕЛОМОВ ПРИ ХБП. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *21*(5), 97-104.
25. Надирова, Ю. И., Жаббаров, О. О., Бобошарипов, Ф. Г., Турсунова, Л. Д., Мирзаева, Г. П., & Надирова, Ю. И. (2023). ОЦЕНКА ЭФФЕКТИВНОСТИ И ОПТИМИЗАЦИЯ ДЕЗАГГРЕГАНТНОЙ ТЕРАПИИ У БОЛЬНЫХ С ИБС.
26. Кодирова, Ш. А. (2023). Особенности Течения Желчно-Каменной Болезни У Больных Ишемической Болезнью Сердца.