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REVIEW

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The cardiovascular system renal regulation

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ABSTRACT

The study of kidney physiology and cardiovascular system physiology has long unveiled several points of contract from which the existence of integrated mechanisms between the two systems has readily been inferred. In conclusion, the need is felt to conduct new studies to explore how the physiologic response to neuro-vegetative stimuli correlates to the renal function level indicated by the glomerular filtration rate (GFR) in a view to demonstrating that a decreased GFR results in cardiovascular alterations whose size is directly proportional to the same GFR reduction.

Keywords: Cardiovascular system physiology, Cardiorenal syndrome, Kidney physiology, Renal nerves, Renal perfusion

The study of the physiology of the kidney and of the cardiovascular system has long unveiled several points of contact from which the existence of integrated mechanisms between the two systems has been readily inferred. The historical foundation of the above integrated mechanisms was laid down by A.C. Guyton who wrote "a renal fraction does exist, i.e., the portion of the total cardiac output that enters the kidney; this fraction has been assessed to be around 21% of the total cardiac output since the total cardiac output of a healthy adult male at rest is about 5600 cc/m and the relevant blood supply to the two kidneys is about 200 cc/m"; this renal fraction may range from 12% to 30% even in healthy subjects at rest (1). For several years this basic notion has suggested that the "cleansing" function of the kidney, which takes place through a process of glomerular capillaries plasma filtration, correlated only with the blood flow rate of the same clusters as a function of the quantity of blood the heart was able to supply to peripheral circulation. This same notion was at the basis of the so-called "pre-renal renal failure" observed in clinical practice, i.e., a renal dysfunction that results from the heart and/or systemic conditions characterized by a decreased cardiac output. On these grounds the kidney was universally thought to be a hemodynamically passive organ whose functional efficiency relied only on the amount of blood received from the heart and whose main function seemed to be confined to either increasing or reducing the glomerular filtration rate in response (and in the same percentage) to either a reduced or increased heart output. However, as early as 1984, Katholi et al reported that parenchymal renal afferent nerve fibers are able to send adenosine-mediated general nerve impulses to the diencephalon and that these impulses result in arterial hypertension with increased plasma norepinephrine levels (2).

In 1987 Katholi completed his studies reporting the occurrence of a "renal reflex", between the renal tissue and the orthosympathetic autonomic nervous system (3).

More recently, Ciriello and de Oliveira (4), Johns (5) and Phillips (6) have reported that the renal afferent nerve fibers in question reach the different levels of the central nervous system thus interacting with other impulses coming from other districts in the genesis of the orthosympathetic descending efferent nerve fibers and participating in the regulation of (i) systemic blood flow, (ii) vascular tone and (iii) arterial hypertension.

Against this background, one first new notion has been added to modern renal physiology under which the kidney is no longer considered as a passive "observer" of the oscillations of the renal blood flow rate that exclusively serves as a filter of the blood is supplied with. Quite the contrary, the kidney is an organ equipped with chemoceptive and mechanoceptive sensors through which the renal blood flow rate increases and decreases and which trigger different amounts of diencephalon-targeted and proximal brainstem-targeted nerve impulses involved in the modulation of the orthosympathetic activity. The above chemoceptive and mechanoceptive sensors result in cardiovascular effects meant to rectify the renal blood flow rate increases and decreases in question by inducing changes in both arterial pressure and heart rate.

This sequence of orthosympathetic efferent impulses from the brainstem diencephalon-proximal areas, which is "also" made of impulses whose generation is "orchestrated" by the kidney itself, reaches the renal tissue by scattering impulses on bundles of nerve fibers that make their way into specific intrarenal areas (afferent arterioles, efferent arterioles, macula densa, distal tubule), gently stimulating the

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specific functions of these latter (7-9). These observations have led to the formulation of a second notion of renal physiology under which the kidney modulates the orthosympathetic systemic function by self-regulating all of its individual functional units and not only parenchymal blood perfusion. Finally, the latest renal physiology (from 2005 to 2008) studies carried out by Xu et al have highlighted the existence of a third hormone produced by the kidney (besides renin and erythropoietin). The production of this hormone, referred to as "renalase", which is able to catabolize noradrenaline and other blood flow catecholamines, is stimulated by the blood concentration of the same catecholamines (10-12). The kidney is therefore able to counter any orthosympathetic activity increases by providing a mechanism of protection against renal and systemic damage from arterial hypertension and heart failure. But the close correlation between heart function and kidney function reported by Guyton (1) was only limited to the relationship between cardiac output and renal blood volume and failed to explain how atherosclerosis and myocardial structural changes could over time result in a decreased renal function. Under Guyton's central model the kidney regulated the extracellular volume with the renin aldosterone mechanism of endothelin and the various antagonists (nitric oxide and natriuretic peptide). In 2005 some authors revised Guyton's model and proposed the "cardio-renal connection" (13). In this new model the renal control of blood volume and blood pressure must be connected to other pathogenic factors (increased renin activity, inflammation, oxidative stress, increased activity of the sympathetic nervous system) which play a synergistic role in the functions of the heart and the kidney. The alteration of one of these factors results in a failure of the entire system which determines the various types of cardio-renal syndromes and reno-cardiac syndromes (13). These pathological conditions are also exacerbated by the processes of cardiomyocytes apoptosis due to toxic and ischemic damage of the myocardium (14). In 2013, the presence of modest reductions in renal function was also reported to be linked to increased cardiac morbidity and mortality, much as coronary damage and left-ventricular diastolic dysfunction were also reported to decrease kidney function. These pathological conditions stem from the need to improve renal perfusion through increased cardiac function, but vascular stress, high blood pressure and increased blood volume that take place in an initial phase in the end result in a damage of the heart and the kidney together (15).

The initial onset of renal damage with subsequent cardiac involvement or, the other way around, the initial onset of a cardiac damage with subsequent renal involvement, determine the different types of cardio-renal syndromes. It is very important to study the various bio-renal and cardiac markers in order to understand the exact sequence of the various syndrome-inducing phenomena and their severity (16).

In conclusion thirty years after A.C. Guyton's seminal studies, modern clinical renal physiology and nephrology consider the kidney as a chemo/mechanoceptive "sensor" which senses systemic hemodynamic oscillations and plays a role in their autonomic regulation in order to fulfill four objectives: (i) ensuring an optimal blood perfusion for glomerular filtration, (ii) regulating and coordinating the activity of its various functional units (afferent arterioles, efferent arterioles, macula densa, distal tubule), (iii) limiting the onset of systemic arterial hypertension, and (iv) playing a proactive cardio-protective role. Therefore, the need is felt to conduct further studies to explore how the physiologic response to autonomic stimuli correlates to the level of renal function indicated by the glomerular filtration rate (GFR) with a view to demonstrating that a decreased GFR results in cardiovascular alterations whose extent is directly proportional to the same GFR reduction.

Disclosures

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References

1. Guyton AG. Trattato di Fisiologia Medica. Piccin Editore. 1977;405.
2. Katholi RE, Whitlow PL, Hageman GR, Woods WT. Intrarenal adenosine produces hypertension by activating the sympathetic nervous system via the renal nerves in the dog. J Hypertens. 1984;2(4):349-359.
3. Katholi RE, Woods WT. Afferent renal nerves and hypertension. Clin Exp Hypertens A. 1987;9(Suppl 1):211-226.
4. Ciriello J, de Oliveira CV. Renal afferents and hypertension. Curr Hypertens Rep. 2002;4(2):136-142.
5. Johns EJ. Angiotensin II in the brain and the autonomic control of the kidney. Exp Physiol. 2005;90(2):163-168.
6. Phillips JK. Pathogenesis of hypertension in renal failure: role of the sympathetic nervous system and renal afferents. Clin Exp Pharmacol Physiol. 2005;32(5-6):415-418.
7. DiBona GF. Neural control of the kidney: functionally specific renal sympathetic nerve fibers. Am J Physiol Regul Integr Comp Physiol. 2000;279(5):R1517-R1524.
8. Denton KM, Luff SE, Shweta A, Anderson WP. Differential neural control of glomerular ultrafiltration. Proceedings Australian Physiological Pharmacol Society. 2004;34:85-91.
9. Eppel GA, Malpas SC, Denton KM, Evans RG. Differential neural control of glomerular ultrafiltration. Proceedings Australian Physiological Pharmacol Society. 2004;34:93-104.
10. Xu J, Li G, Wang P, et al. Renalase is a novel, soluble monoamine oxidase that regulates cardiac function and blood pressure. J Clin Inv. 2005;115(5):1275-1280.
11. Xu J, Desir GV. Renalase, a new renal hormone: its role in health and disease. Curr Opin Nephrol Hypertens. 2007;16: 373-378.
12. Li G, Xu J, Wang P, et al. Catecholamines regulate the activity, secretion, and synthesis of renalase. Circulation. 2008;117(10): 1277-1282.
13. Bongartz LG, Cramer MJ, Doevendans PA, Joles JA, Braam B. The severe cardiorenal syndrome: 'Guyton revisited'. Eur Heart J. 2005;26(1):11-17.
14. Virzì GM, Clementi A, Ronco C. Cellular apoptosis in the cardiorenal axis. Heart Fail Rev. 2016;21(2):177-189.
15. Tumlin JA, Costanzo MR, Chawla LS, et al. Cardiorenal syndrome type 4: insights on clinical presentation and pathophysiology from the eleventh consensus conference of the Acute Dialysis Quality Initiative (ADQI). Contrib Nephrol. 2013;182: 158-173.
16. Di Lullo L, Floccari F, Rivera R, et al. Valutazione della funzione ventricolare destra in pazienti affetti da malattia renale cronica in stadio I-V NKF. G Ital Nefrol. 2013;30(5):1-29.