Hypertension Research (2024) 47:548–550
https://doi.org/10.1038/s41440-023-01508-3

COMMENT

Association between serum irisin levels and blood pressure in patients undergoing hemodialysis

Kengo Azushima[1] · Kouichi Tamura[1]

Received: 29 September 2023 / Revised: 11 October 2023 / Accepted: 15 October 2023 / Published online: 10 November 2023

Keywords Blood pressure · Hemodialysis · Irisin

Irisin is a novel muscle-secreted hormone (myokine) that is produced through the cleavage of a transmembrane protein, fibronectin type III domain-containing protein 5 (FNDC-5) [1]. Although the exact details of FNDC-5 cleavage are not completely understood, a disintegrin and metalloproteinase (ADAM) family member, ADAM-10 has been proposed as a candidate protease that cleaves FNDC-5 [2]. A previous study demonstrated that angiotensin II upregulates ADAM-10, indicating the involvement of the renin-angiotensin system in irisin production [2]. FNDC-5 is mainly expressed in muscle tissues, including skeletal and cardiac muscles, making muscle the primary source of irisin production [3, 4]. Notably, other tissues, such as liver, thyroid, adrenal grand, white adipose tissue, and central nervous system, also express FNDC-5 and can produce irisin [1]. Originally, irisin was identified as a mediator of exercise-induced metabolic improvements, attributable to an increase in energy expenditure due to the browning of white adipose tissue [3]. However, an increasing number of studies have explored the physiological and pathophysiological roles of irisin in the regulation of blood pressure (BP) and hypertension.

Animal studies found that irisin administration led to a significant reduction in BP in both Zucker diabetic fatty rats and spontaneously hypertensive rats, accompanied by improvements in renal sodium retention, arterial endothelial dysfunction, and oxidative stress within the paraventricular nucleus [5–7]. In humans, it seems to have been established that circulating irisin levels in patients with chronic kidney disease are significantly decreased compared to those in healthy controls [8, 9]. Conversely, clinical studies have reported conflicting results regarding the association between circulating irisin levels and BP in patients with chronic kidney disease [10–13].

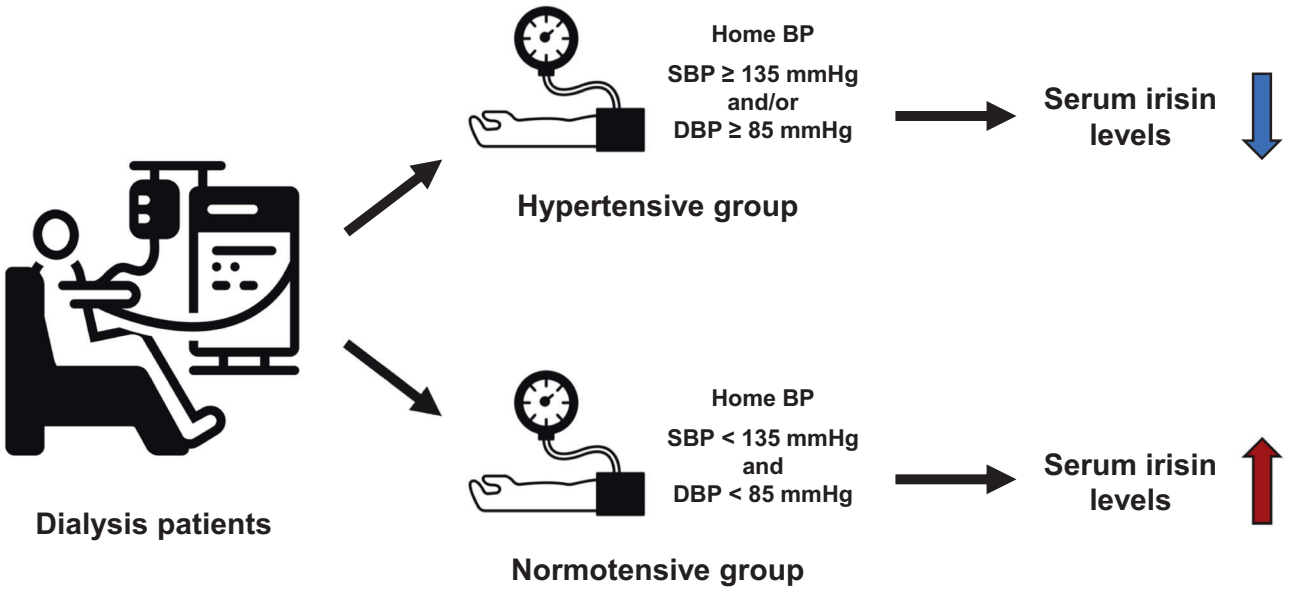
The present study by Wang et al. [14] evaluated the clinical associations between serum irisin levels and BP in 350 patients undergoing dialysis at the Xuanwu Hospital Capital Medical University. This study included patients aged >18 years who were undergoing dialysis for >3 months and agreed to participate. Patients with cancer, overt infection, or significant clinical events within 3 months before study enrollment were excluded. In total, 300 patients were found to be eligible for inclusion in the study and were thus enrolled. The average BP was determined based on the morning and evening BP levels checked at home for 7 consecutive days to exclude the effects of BP variability in the peri-dialysis period. The participants were categorized into hypertensive (systolic BP ≥ 135 mmHg and/or diastolic BP ≥ 85 mmHg) and normotensive (systolic BP < 135 mmHg and diastolic BP < 85 mmHg) groups based on the home BP levels, regardless of the use of anti-hypertensive agents. Compared to the normotensive group, the hypertensive group had significantly lower serum irisin levels. Pearson correlation analysis revealed that serum irisin levels were negatively correlated with systolic BP. Furthermore, multivariate analysis demonstrated that lower serum irisin levels were independently associated with higher BP levels after adjustment for confounders.

Few clinical studies have provided evidence regarding the association between circulating irisin levels and BP. The present study by Wang et al. provides new insights into this association among patients undergoing hemodialysis. However, given the cross-sectional design of the study [10–13], the causal relationship between circulating irisin levels and BP remains unclear. In addition, given the

✉ Kengo Azushima
azushima@yokohama-cu.ac.jp

[1] Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Graphical Opinion



- Hypertensive group had significantly lower serum irisin levels compared to normotensive group.
- Serum irisin levels were negatively correlated with systolic blood pressure.
- Lower serum irisin levels were independently associated with higher blood pressure levels.

conflicting results of previous clinical studies, it is possible that the clinical significance of circulating irisin levels varies among disease types. Therefore, further evidence is needed to clarify these uncertainties, which would enhance our understanding of the mechanisms underlying hypertension and facilitate the development of novel antihypertensive agents.

Acknowledgements We thank Textcheck for editing and reviewing the English in this manuscript.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Bao JF, She QY, Hu PP, Jia N, Li A. Irisin, a fascinating field in our times. Trends Endocrinol Metab. 2022;33:601–13.
2. Yu Q, Kou W, Xu X, Zhou S, Luan P, Xu X, et al. FNDC5/Irisin inhibits pathological cardiac hypertrophy. Clin Sci. 2019;133:611–27.
3. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012;481:463–8.
4. Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. Metabolism. 2012;61:1725–38.
5. Huang Y, Chen Q, Jiang Q, Zhao Z, Fang J, Chen L. Irisin lowers blood pressure in Zucker diabetic rats by regulating the functions of renal angiotensin II type 1 receptor via the inhibition of the NF-κB signaling pathway. Peptides. 2022;147:170688.
6. Fu J, Han Y, Wang J, Liu Y, Zheng S, Zhou L, et al. Irisin lowers blood pressure by improvement of endothelial dysfunction via AMPK-Akt-eNOS-NO pathway in the spontaneously hypertensive rat. J Am Heart Assoc. 2016;5:e003433.
7. Huo CJ, Yu XJ, Sun YJ, Li HB, Su Q, Bai J, et al. Irisin lowers blood pressure by activating the Nrf2 signaling pathway in the hypothalamic paraventricular nucleus of spontaneously hypertensive rats. Toxicol Appl Pharmacol. 2020;394:114953.
8. Wen MS, Wang CY, Lin SL, Hung KC. Decrease in irisin in patients with chronic kidney disease. PLoS One. 2013;8:e64025.
9. Gan W, Chen W, Li T, Shao D, Xu F, Huo S, et al. Circulating irisin level in chronic kidney disease patients: a systematic review and meta-analysis. Int Urol Nephrol. 2022;54:1295–302.
10. Liu JJ, Liu S, Wong MD, Tan CS, Tavintharan S, Sum CF, et al. Relationship between circulating irisin, renal function and body composition in type 2 diabetes. J Diabetes Complications. 2014;28:208–13.

11. Ebert T, Focke D, Petroff D, Wurst U, Richter J, Bachmann A, et al. Serum levels of the myokine irisin in relation to metabolic and renal function. Eur J Endocrinol. 2014;170:501–6.
12. Lee MJ, Lee SA, Nam BY, Park S, Lee SH, Ryu HJ, et al. Irisin, a novel myokine is an independent predictor for sarcopenia and carotid atherosclerosis in dialysis patients. Atherosclerosis. 2015;242:476–82.
13. Kałużna M, Pawlaczyk K, Schwermer K, Hoppe K, Człapka-Matyasik M, Ibrahim AY, et al. Adropin and irisin: new biomarkers of cardiac status in patients with end-stage renal disease? A preliminary study. Adv Clin Exp Med. 2019;28:347–53.
14. Wang PX, Fan ZJ, Wu LY, Wang SY, Zhang JL, Dong XT, et al. Serum irisin levels are negatively associated with blood pressure in dialysis patients. Hypertens Res. 2023. https://doi.org/10.1038/s41440-023-01449-x.