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Multiple urinary peptides are associated with hypertension: a link to molecular pathophysiology
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Abstract

Objectives: Hypertension is a common condition worldwide; however, its underlying mechanisms remain largely unknown. This study aimed to identify urinary peptides associated with hypertension to further explore the relevant molecular pathophysiology. **Methods:** Peptidome data from 2876 individuals without end-organ damage were retrieved from the Human Urinary Proteome Database, belonging to general population (discovery) or type 2 diabetic (validation) cohorts. Participants were divided based on systolic blood pressure (SBP) and diastolic BP (DBP) into hypertensive (SBP 140 mmHg and/or DBP 90 mmHg) and normotensive (SBP <120 mmHg and DBP <80 mmHg, without antihypertensive treatment) groups. Differences in peptide abundance between the two groups were confirmed using an external cohort (n = 420) of participants without end-organ damage, matched for age, BMI, eGFR, sex, and the presence of diabetes. Furthermore, the association of the peptides with BP as a continuous variable was investigated. The findings were compared with peptide biomarkers of chronic diseases and bioinformatic analyses were conducted to highlight the underlying molecular mechanisms. **Results:** Between hypertensive and normotensive individuals, 96 (mostly COL1A1 and COL3A1) peptides were found to be significantly different in both the discovery (adjusted) and validation (nominal significance) cohorts, with consistent regulation. Of these, 83 were consistently regulated in the matched cohort. A weak, yet significant, association between their abundance and standardized BP was also observed. **Conclusion:** Hypertension is associated with an altered urinary peptide profile with evident differential regulation of collagen-derived peptides. Peptides related to vascular calcification and sodium regulation were also affected. Whether these modifications reflect the pathophysiology of hypertension and/or early subclinical organ damage requires further investigation. Copyright © 2024 Wolters Kluwer Health, Inc. All rights reserved.

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blood pressure; CE-MS; hypertension; peptides; urine

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