IRINE ANDRONIKASHVILI, ALEXANDRE TAVARTKILADZE, DIANA LABARTKAVA, SOPHIE TATISHVILI, NATO PANTSULAIA

SERUM ALDOSTERONE AND PLASMA RENIN ACTIVITY PROFILES IN DIAGNOSING SALT SENSITIVITY IN METABOLIC SYNDROME

V.Bakhutashvili Institute of Medical Biotechnology, Tbilisi State Medical University; Institute for Personalized Medicine; Tbilisi, Georgia

Doi: https://doi.org/10.52340/jecm.2025.05.13

ირინე ანდრონიკაშვილი, ალექსანდრე თავართქილაძე, დიანა ლაბარტყავა, სოფიო ტატიშვილი, ნატო ფანცულაია

შრატის ალდოსტერონისა და პლაზმის რენინის აქტივობის პროფილები მეტაბოლური სინდრომის დროს მარილმგრძნობელობის დიაგნოსტიკაში

ვ. ბახუტაშვილის სახ. სამედიცინო ბიოტექნოლოგიის ინსტიტუტი, თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი; პერსონალიზებული მედიცინის ინსტიტუტი; თბილისი საქართველო

რეზიუმე

შესავალი: მარილისმგრძნობელობა (SS) მნიშვნელოვან როლს თამაშობს მეტაბოლურ სინდრომთან (MetS) ასოცირებული ჰიპერტენზიის დროს. მოცემული კვლევა იკვლევს შრატის ალდოსტერონისა და პლაზმის რენინის აქტივობის (PRA) დიაგნოსტიკურ მნიშვნელობას SS-ის დასადგენად MetS-ის მქონე პაციენტებში.

მეთოდები: 120 საშუალო ასაკის MetS-ის მქონე პაციენტს ჩაუტარდა მარილმგრძნობელობის ტესტი. ნატრიუმის დაბალი და მაღალი შემცველობის ფაზების შემდეგ განისაზღვრა არტერიული წნევა (BP), შრატის ალდოსტერონი და PRA. მარილისმგრძნობელობას ვსაზღვრავდით, როგორც საშუალო არტერიული წნევის (MAP) ≥10 მმHg მატებას. ასევე განისაზღვრებოდა ალდოსტერონ-რენინის თანაფარდობა (ARR).

შედეგები: მონაწილეთა 39.2% აღმოჩნდა მარილმგრძნობელი. SS ჯგუფში მაღალი ნატრიუმის მიღების პირობებში აღინიშნებოდა PRA-ს დათრგუნვა და ალდოსტერონის მატება. ARR-მ აჩვენა მაღალი პროგნოზული მნიშვნელობა (AUC 0.87).

დასკვნები: ნატრიუმის დატვირთვის პირობებში ალდოსტერონისა და PRA-ს პროფილების განსაზღვრა ეფექტური საშუალებაა SS ფენოტიპის იდენტიფიცირებისა MetS-ის მქონე პაციენტებში, რაც მკურნალობისადმი პერსონალიზებული მიდგომის პერსპექტივას ხდის შესაძლებელს.

Introduction. The impact of salt sensitivity on blood pressure may not be well appreciated, particularly in the context of the Metabolic Syndrome (MetS) framework, where the risk of cardiovascular disease is elevated. MetS includes central obesity, dyslipidemia, insulin resistance, and hypertension. These subjects typically have sodium retention, reduced renal sodium handling, impaired renal sodium handling, some degree of endothelial dysfunction and increased RAAS activity [2,3,9].

The underlying mechanism of increased salt-sensitivity among individuals with the metabolic syndrome is not fully understood, but as it seems, the renin-angiotensin-aldosterone system (RAAS) plays a central role. Non-suppressible serum aldosterone, in conjunction with suppressed plasma renin activity, leads to sodium intake violating some form of feedback system. Thus, identifying biomarkers associated with the RAAS may play an important role in both identifying salt-sensitive individuals and developing personalized treatment methods [4,5,7].

This study aims to investigate the diagnostic utility of serum aldosterone, PRA, and their ratio (ARR) in diagnosing salt sensitivity among patients with MetS. Identifying SS phenotypes could inform personalized dietary and pharmacologic interventions, ultimately reducing cardiovascular risk.

Methods. The research included 120 middle-aged Georgian participants aged 38-62 years who received a MetS diagnosis according to IDF criteria. Written informed consent was obtained. The study

excluded participants who had chronic kidney disease or secondary hypertension or adrenal tumors or were taking RAAS-modifying agents. The research design included two dietary stages which started with a 7-day low-sodium diet (Na <50 mmol/day) followed by a 7-day high-sodium diet (Na >200 mmol/day). How the patient adhered to the diet was monitored via 24-hour urinary sodium excretion. Blood pressure was measured at the end of each phase by using automated oscillometric devices (mean of 3 readings), and fasting blood samples were collected for PRA (measured by radioimmunoassay) and serum aldosterone (measured via chemiluminescence immunoassay). The ARR was calculated. Salt sensitivity was defined as a ≥10 mmHg increase in mean arterial pressure (MAP) between the two phases [6]. Statistical analysis was conducted using SPSS v26. Continuous variables were compared using Student's t-test or Mann–Whitney U test, depending on normality. ROC curves were constructed to evaluate the diagnostic value of ARR, PRA, and aldosterone levels.

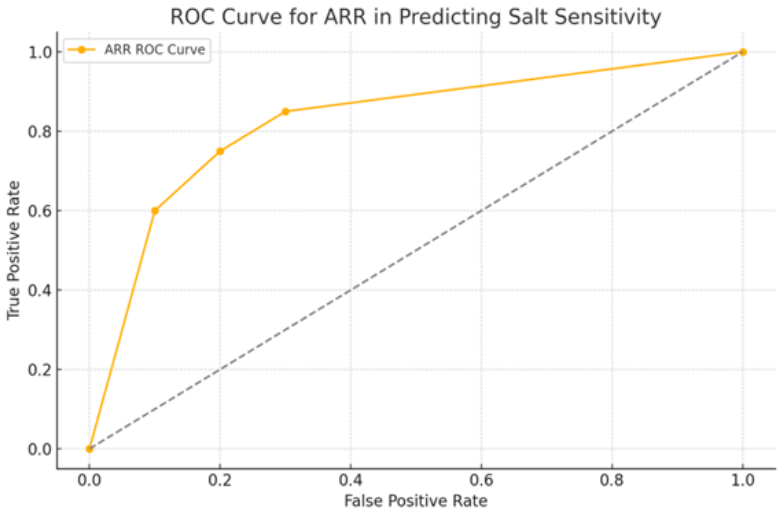
Results. 47 (39.2%) of the 120 participants satisfied the requirements for salt sensitivity. There were no significant differences in age, body mass index, gender, and baseline blood pressure between salt-resistant and SS individuals. Under high-sodium conditions, SS patients exhibited significantly lower PRA (0.42 ± 0.19 ng/mL/h) compared to salt-resistant participants (1.12 ± 0.38 ng/mL/h). Aldosterone levels were significantly higher in SS individuals (21.7 ± 5.3 ng/dL vs. 13.4 ± 3.1 ng/dL). The resulting ARR was markedly elevated in the SS group (Table 1).

Table 1. Comparison of RAAS Biomarkers in Salt-Sensitive and Salt-Resistant Participants

Group	PRA (ng/mL/h)	Aldosterone (ng/dL)	ARR	MAP Increase (mmHg)
Salt-Sensitive	0.42 ± 0.19	21.7 ± 5.3	51.7	13.2 ± 2.1
Salt-Resistant	1.12 ± 0.38	13.4 ± 3.1	11.9	3.7 ± 1.4

ROC curve analysis revealed that ARR had the highest diagnostic performance with an AUC of 0.87 (95% CI: 0.80–0.92). At a cutoff of ARR > 25, the sensitivity was 82.3% and specificity was 78.6% (Fig 1).

Figure 1. ROC curve demonstrating diagnostic performance of ARR under high-sodium conditions (AUC=0.87)



Discussion. The findings from our study endorse the application of specific RAAS biomarkers, in particular the aldosterone-renin ratio, for accurately pinpointing salt-sensitive individuals within the

metabolic syndrome (MetS) framework. The patterns of suppressed PRA and inappropriately elevated aldosterone concentration during high sodium conditions are suggestive of altered sodium balance, likely from intrinsic renal sodium retention [1,8]. Our study outcomes are consistent with previous reports that linked salt sensitivity with lower renin phenotypes and inappropriate aldo persistency. However, this model had not previously been studied in MetS, a condition where the prevalence of SS may be markedly due to coexisting hybrid metabolic and endocrine imbalances [10]. These findings may enable outpatient categorization of individuals based on defined profiles of RAAS biomarkers, thus tailoring dietary sodium recommendations and identifying candidates for treatment with mineralocorticoid receptor antagonists.

Some of the study limitations include a relatively short length of the dietary phases, absence of 24-hour ambulatory BP monitoring, and a lack of long-term cardiovascular outcomes.

Conclusion. Based on our study, we can assume that serum aldosterone, PRA, and especially their ratio, can be used as a simple and effective diagnostic tool to determine salt sensitivity in patients with metabolic syndrome. The implementation of these data as biomarkers of salt sensitivity in clinical practice may contribute to the development of individualized strategies for hypertension management and cardiovascular risk reduction in this population.

References:

1. Gaddam KK, et al. (2008). Aldosterone excess and resistant hypertension. Curr Hypertens Rep, 10(6), 430–435.
2. Grassi G, et al. (2016). Sympathetic overdrive and cardiovascular risk in metabolic syndrome. Hypertens Res, 39(3), 159–167.
3. Kawasaki T, et al. (1993). Salt sensitivity of blood pressure in humans. Hypertension, 21(5), 600–606.
4. Lifton RP, et al. (2001). Molecular mechanisms of human hypertension. Cell, 104(4), 545–556.
5. Sanada H, et al. (2006). Gene polymorphisms and the salt-sensitive hypertension phenotype. Hypertens Res, 29(9), 587–593.
6. Sullivan JM, et al. (1980). Hemodynamic effects of dietary sodium in man: a preliminary report. Hypertension, 2(5), 506–514
7. Pimenta E, et al. (2008). Low-renin hypertension: a review of mechanisms and therapeutic options. J Clin Hypertens, 10(6), 394–403.
8. Vongpatanasin W. (2014). RAAS suppression in salt-sensitive hypertension: friend or foe? Hypertension, 64(1), 20–21.
9. Weinberger MH, et al. (2001). Salt sensitivity: An important but neglected cardiovascular risk factor. J Hum Hypertens, 15(12), 755–763.
10. Yuan YE, Haas AV, Rosner B, Williams GH, McDonnell ME, Adler GK. (2025) The renin-angiotensin-aldosterone system and salt sensitivity of blood pressure offer new insights in obesity phenotypes. Obesity (Silver Spring). 33(2):321-330.

IRINE ANDRONIKASHVILI, ALEXANDRE TAVARTKILADZE, DIANA LABARTKAVA, SOPHIE TATISHVILI, NATO PANTSULAIA

SERUM ALDOSTERONE AND PLASMA RENIN ACTIVITY PROFILES IN DIAGNOSING SALT SENSITIVITY IN METABOLIC SYNDROME

V.Bakhutashvili Institute of Medical Biotechnology, Tbilisi State Medical University;
Institute for Personalized Medicine; Tbilisi, Georgia

SUMMARY

Background: Salt sensitivity (SS) is a major contributor to hypertension in the context of Metabolic Syndrome (MetS). This study evaluated serum aldosterone and plasma renin activity (PRA) as diagnostic tests for SS in the clinical context of MetS.

Methods: 120 met individuals with MetS participated in a dietary sodium protocol. Blood pressure (BP), serum aldosterone, and PRA were conducted in the high- and low-sodium phases of the study. Salt Sensitivity was defined as a increase in MAP of ≥10 mmHg. An aldosterone-renin ratio (ARR) was considered.

Results: 39.2% of participants were salt sensitive. The SS group had lower PRA and higher aldosterone levels relative to baseline during the high sodium condition. ARR held a high degree of predictive value of SS (AUC 0.87).

Conclusions: Aldosterone and PRA response to dietary sodium challenge identify SS phenotype of MetS and are helpful for complexities of precision care.

Keywords: Salt sensitivity, Metabolic syndrome, Aldosterone, Plasma renin, Hypertension, ARR