

A Clinical Validation Study and the Psychological Implications of Early Risk Detection: Predictive Biomarkers for Resistant Hypertension

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The purpose of this prospective cohort study was to determine the predictive capability of a set of biomarkers to detect patients who will ultimately develop resistant hypertension. Another objective was also to evaluate whether early biomarker risk stratification could reduce the psychological uncertainty associated with a "wait-and-see" treatment strategy. This study was carried out between February and October 2025 in specialized cardiovascular care centers in Amman and Irbid, Jordan. A total of 240 patients aged between 18 and 70 years with hypertension either newly diagnosed or uncontrolled by two antihypertensive drugs underwent standard stepped treatment. Pre-intervention tests included the determination of the plasma aldosterone renin ratio, N-terminal pro-brain natriuretic peptide, high-sensitivity C-reactive protein, plasma sodium, and urine sodium-to-creatinine ratio. Resistance to treatment of hypertension was diagnosed based on the following: blood pressure readings of 140/90 mmHg or higher despite adherence to treatment using three full-dose antihypertensive drugs of different types, which included a diuretic, or blood pressure necessitating the use of four or more drugs to achieve control, documented at 24 weeks of follow-up. Patients were asked about compliance and drug-taking at each follow-up and those that failed compliance checks were excluded from resistance to treatment of hypertension. Resistant hypertension after 24 weeks (uncontrolled hypertension despite use of three drugs or requiring four antihypertensives including a diuretic) served as the primary outcome. Of the 210 patients that completed follow-up visits, 48 (22.9%) had resistant hypertension. The aldosterone-to-renin ratio (AR) test, with an area under the curve of 0.79, showed the highest individual predictive capacity. Combining AR, NT-proBNP, hs-CRP, baseline systolic blood pressure, body mass index, and GFR results in an area under the curve of 0.86 (confidence interval: 0.91–0.81), a sensitivity of 81.3%, specificity of 82.7%, and negative predictive value of 92.7%. A negative predictive value of such an extent provides considerable assurance in the clinical setting, thereby helping rule out any form of treatment resistance. In a multivariate model, AR, NT-proBNP, hs-CRP, baseline systolic blood pressure, body mass index, and functional decline were found to be significant independent predictors of treatment resistance. Taken together, these results indicate that a baseline biomarker profile is able to precisely determine those individuals at high risk of developing resistant hypertension prior to the beginning of treatment. In this way, by adopting a preventive rather than reactive strategy, whereby the risk profile of each patient is evaluated before treatment, this solution makes clinical decision making easier while also reducing the psychological burden of prolonged, uncontrolled hypertension.

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