The association between sleep quality metrics and resistant hypertension progression

Asociación entre la calidad del sueño y la progresión de la hipertensión resistente

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Abstract

Resistant hypertension (RH) poses a significant cardiovascular risk, particularly in regions like Uzbekistan with rising prevalence, yet modifiable factors influencing its progression remain underexplored. Sleep quality disruptions may accelerate RH through nocturnal blood pressure surges and inflammation, but evidence from Central Asia is lacking. This study conducted from March 2024 to September 2025 at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Tashkent, we followed 320 adults (mean age 58.4 years, 50.6% male) with RH. Sleep was assessed via Pittsburgh Sleep Quality Index (PSQI) and actigraphy at baseline and 6-month intervals. RH progression was defined by 24-hour ambulatory BP increase ≥10 mmHg systolic, medication escalation, or organ damage. Multivariable Cox regression evaluated associations, adjusting for age, BMI, diabetes, and smoking. Over 18 months, 92 (28.8%) progressed. Progressors had poorer baseline PSQI (10.2 ± 3.1 vs. 7.9 ± 3.2, p<0.001), sleep efficiency (72% ± 11% vs. 81% ± 10%, p<0.001), and hs-CRP (3.2 ± 1.8 mg/L vs. 2.1 ± 1.4, p=0.002). Adjusted HRs were 1.18 (95% CI 1.10-1.26) per PSQI unit and 1.32 (1.20-1.46) per 5% efficiency drop (both p<0.001; c-statistic 0.78). Kaplan-Meier analysis showed early divergence (log-rank p<0.001). The findings shows, Poor sleep quality robustly predicts RH progression in Uzbek patients, highlighting a modifiable target for intervention. Routine PSQI screening could refine management in resource-limited settings.

Keywords: Resistant Hypertension, Sleep Quality, PSQI, Progression

Resumen

La hipertensión resistente (HR) representa un riesgo cardiovascular significativo, especialmente en regiones como Uzbekistán, donde su prevalencia está en aumento. Sin embargo, los factores modificables que influyen en su progresión aún no se han explorado en profundidad. Las alteraciones en la calidad del sueño podrían acelerar la HR mediante aumentos repentinos de la presión arterial nocturna e inflamación, pero la evidencia proveniente de Asia Central es escasa. En este estudio, realizado entre marzo de 2024 y septiembre de 2025 en el Centro Médico Científico-Práctico Especializado Republicano de Cardiología en Tashkent, se realizó un seguimiento a 320 adultos (edad promedio: 58,4 años; 50,6 % hombres) con HR. El sueño se evaluó mediante el Índice de Calidad del Sueño de Pittsburgh (PSQI) y actigrafía al inicio del estudio y a intervalos de 6 meses. La progresión de la HR se definió por un aumento de la presión arterial ambulatoria de 24 horas ≥10 mmHg sistólica, un aumento en la medicación o daño orgánico. La regresión de Cox multivariable evaluó las asociaciones, ajustando por edad, IMC, diabetes y tabaquismo. Durante 18 meses, 92 (28,8%) progresaron. Los que progresaron tuvieron peores valores basales de PSQI (10,2 ± 3,1 vs. 7,9 ± 3,2, p<0,001), eficiencia del sueño (72% ± 11% vs. 81% ± 10%, p<0,001) y hs-CRP (3,2 ± 1,8 mg/L vs. 2,1 ± 1,4, p=0,002). Los HR ajustados fueron 1,18 (IC del 95%: 1,10-1,26) por unidad de PSQI y 1,32 (1,20-1,46) por cada 5% de disminución de la eficiencia (ambos p<0,001; estadístico c: 0,78). El análisis de Kaplan-Meier mostró una divergencia temprana (log-rank p<0,001). Los hallazgos demuestran que la mala calidad del sueño predice de forma robusta la progresión de la hipertensión resistente en pacientes uzbekos, lo que pone de relieve un objetivo modificable para la intervención. La evaluación rutinaria mediante el PSQI podría optimizar el manejo en entornos con recursos limitados.

Palabras clave: Hipertensión resistente, Calidad del sueño, PSQI, Progresión

Introduction

Hypertension is one of the leading contributors to cardiovascular disease worldwide, affecting millions and imposing a heavy burden on healthcare systems[1]. Resistant hypertension (RH), defined as blood pressure that remains elevated despite adherence to three or more antihypertensive medications at optimal doses, represents a particularly challenging subset, with progression often leading to severe complications like stroke, heart failure, and kidney disease[2]. In Uzbekistan, where cardiovascular conditions account for nearly half of all deaths, the prevalence of RH is alarmingly high, yet local data on its modifiable risk factors remain scarce. This gap underscores the urgent need for targeted research that explores everyday influences on disease progression[3]. Sleep, a fundamental physiological process, has emerged as a potential modulator, yet its specific role in RH advancement in this region has not been adequately examined[4]. Our study seeks to bridge this void by investigating how sleep quality metrics correlate with RH progression among Uzbek patients.

Sleep quality is more than just feeling rested; it's a complex interplay of duration, efficiency, disturbances, and subjective satisfaction that profoundly impacts overall health. Poor sleep has long been linked to metabolic disruptions, inflammation, and autonomic nervous system imbalances, all of which can exacerbate hypertension[5]. In the context of RH, where standard treatments fall short, understanding sleep's contribution could unlock new preventive strategies[6]. Uzbekistan's unique demographic marked by rapid urbanization, dietary shifts toward high-sodium processed foods, and cultural norms around late-night social activities may amplify sleep deficits, potentially accelerating RH. Preliminary global evidence suggests that fragmented sleep patterns increase sympathetic activity and endothelial dysfunction[7], but these findings need validation in understudied populations like ours. By focusing on quantifiable sleep metrics, this research aims to provide actionable insights for clinicians managing RH in resource-limited settings.

The progression of RH is not merely a matter of persistent high blood pressure; it often signals underlying vascular remodeling and organ damage that standard monitoring misses[8]. Studies from Western cohorts indicate that patients with RH experience a 50% higher risk of cardiovascular events compared to those with controlled hypertension, yet progression rates vary widely due to lifestyle and environmental factors[9]. In Uzbekistan, limited access to advanced diagnostics and a healthcare system strained by post-Soviet transitions exacerbate this issue, with many patients progressing to end-stage complications before intervention. Sleep disturbances,

such as insomnia or sleep apnea, could serve as early harbingers, influencing RH through mechanisms like nocturnal hypertension spikes and oxidative stress[10]. This study is essential because it targets these interactions head-on, offering a pathway to integrate sleep assessments into routine RH care protocols.

Global epidemiological data highlight sleep's bidirectional relationship with hypertension. Short sleep duration raises systolic blood pressure by up to 5 mmHg, while poor quality amplifies renin-angiotensin system activity[11]. However, most research clusters in high-income countries, overlooking regions like Central Asia where sleep hygiene is compromised by economic pressures and irregular work shifts[12]. In Uzbekistan, over 40% of adults experience poor sleep, correlating with rising hypertension rates, but no studies have dissected this in RH specifically. The necessity of our work lies in its potential to inform public health policies, such as community-based sleep education programs tailored to local lifestyles[13]. By quantifying metrics like sleep latency and awakenings, we can pinpoint thresholds that predict RH worsening, empowering early intervention.

Resistant hypertension's stubborn nature demands a multifaceted approach, and sleep emerges as an overlooked pillar. Traditional risk factors obesity, salt intake, non-adherence explain only part of the variance in progression[14]; emerging evidence implicates sleep fragmentation in sustaining elevated nighttime blood pressure, a key driver of target-organ damage. Uzbekistan's context adds layers of complexity: harsh continental climates disrupt circadian rhythms, and traditional diets heavy in fats may compound sleep-related insulin resistance. Without targeted investigations, clinicians here rely on generic guidelines ill-suited to these realities[15]. This research addresses that imperative by linking objective sleep data to RH trajectories, potentially reducing progression rates through simple, cost-effective sleep optimization strategies.

The clinical implications of unraveling sleep-RH connections are profound, particularly in low-resource settings like Uzbekistan. Ambulatory blood pressure monitoring already reveals nocturnal patterns in RH patients, but integrating polysomnography-derived sleep metrics could refine risk stratification[16]. Prior studies, such as those from the SPRINT trial, hint at sleep's role in treatment resistance, yet they lack ethnic diversity. Our Uzbek cohort, drawn from diverse urban and rural areas, fills this niche, highlighting how cultural factors like evening tea-drinking rituals affect sleep onset. The urgency stems from rising RH incidence projected to double by 2030 in Central Asia necessitating research that translates to bedside tools, like validated sleep questionnaires for primary care.

Many investigations rely on self-reported sleep, prone to bias, whereas objective metrics from actigraphy or questionnaires like the Pittsburgh Sleep Quality Index (PSQI) offer precision[2,7,10,12,17]. In Uzbekistan, where wearable tech penetration is low, our hybrid approach ensures feasibility while maintaining rigor. Progression of RH, often gauged by escalating medication needs or albuminuria, intertwines with sleep via hypoxia-induced vasoconstriction in undiagnosed apnea cases[18]. By establishing these associations locally, we pave the way for screening protocols that could halve cardiovascular events, underscoring the study's public health imperative.

Uzbekistan's healthcare landscape amplifies the need for this investigation. With hypertension clinics overwhelmed and specialists scarce outside Tashkent, identifying sleep as a progression modifier could democratize care. Evidence from analogous populations in Eastern Europe shows sleep interventions lowering blood pressure by 10-15 mmHg in resistant cases, a game-changer here. Yet, without baseline data on sleep quality metrics efficiency below 85% or disturbances exceeding three nights weekly we risk perpetuating ineffective management. This work's novelty lies in its prospective design, tracking real-world progression to yield evidence-based recommendations for national guidelines.

The broader scientific discourse on chronobiology supports our focus; circadian misalignment from poor sleep dysregulates vascular tone, a core RH pathology[19]. Animal models confirm that sleep restriction accelerates aortic stiffness, mirroring human RH endpoints[7,8]. In human terms, Uzbek patients' profiles often involving shift work in agriculture or industry mirror these stressors. The necessity arises from stalled progress in RH therapies; despite new agents like finerenone, lifestyle levers like sleep remain untapped. Our study promises to elevate sleep from afterthought to cornerstone, fostering interdisciplinary collaborations between cardiologists and sleep specialists.

Finally, this research holds transformative potential for Uzbekistan and beyond, addressing a critical evidence gap in global RH literature dominated by Western data. By demonstrating how sleep quality metrics predict progression potentially via inflammatory pathways like IL-6 elevation we advocate for holistic management. The urgency is clear: unchecked RH progression drains economies and lives, yet sleep, a universal modifiable factor, offers hope. Through rigorous analysis in our local cohort, we not only illuminate mechanisms but also equip policymakers with data to prioritize sleep health in hypertension control strategies, ultimately curbing this epidemic.

Study Participants

We carried out a prospective cohort study over 18 months, from March 2024 to September 2025, at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Tashkent, Uzbekistan. We enrolled 320 adults aged 40-75 years diagnosed with resistant hypertension, confirmed by office blood pressure readings above 130/80 mmHg despite treatment with at least three antihypertensive drugs, including a diuretic, at optimal doses. Participants came from both urban Tashkent clinics and rural outpatient centers in the Tashkent region to capture a mix of lifestyles. Exclusion criteria included secondary hypertension causes like renal artery stenosis, recent stroke or myocardial infarction within six months, severe comorbidities such as advanced chronic kidney disease (eGFR <30 mL/min), and current use of continuous positive airway pressure for sleep apnea. All patients provided informed consent, and we aimed for a balanced cohort with roughly equal gender distribution, 162 men and 158 women, reflecting Uzbekistan's hypertension demographics.

Sleep Quality Assessment and RH Progression Monitoring

Sleep quality metrics were evaluated using the Pittsburgh Sleep Quality Index (PSQI) questionnaire, administered at baseline and every six months, alongside wrist actigraphy (Actiwatch Spectrum Plus, Philips Respironics) worn for seven consecutive nights per interval. PSQI scores ranged from 0 to 21, with higher values indicating poorer sleep; components included subjective quality, latency, duration, efficiency, disturbances, medication use, and daytime dysfunction. Actigraphy provided objective data on total sleep time, wake after sleep onset, and fragmentation index. For RH progression, we tracked changes via 24-hour ambulatory blood pressure monitoring (ABPM, Mobil-O-Graph NG) at baseline, 9 months, and 18 months, defining progression as a sustained increase in mean 24-hour systolic BP ≥10 mmHg, addition of a fourth medication, or new evidence of target-organ damage like left ventricular hypertrophy on echocardiography. Blood samples were drawn for biomarkers such as hs-CRP and aldosterone-renin ratio to contextualize inflammatory and neurohormonal shifts.

Statistical Analysis

Data analysis relied on SPSS version 27.0 and R software (version 4.3.1). We described baseline characteristics using means with standard deviations for continuous variables and frequencies for categorical ones, checked for normality with Shapiro-Wilk tests. Between-group comparisons employed independent t-tests or Mann-Whitney U tests as appropriate, and chi-square tests for proportions. To model associations between sleep metrics and RH progression, we used multivariable Cox proportional hazards regression, adjusting for confounders like age, sex, BMI, smoking status, diabetes, and baseline BP. Time-to-progression served as the primary outcome, with hazard ratios and 95% confidence intervals reported. We assessed model fit via Schoenfeld residuals and Kaplan-Meier curves for survival analysis. Subgroup analyses explored interactions by age and sex, with a two-sided p-value <0.05 deemed significant. Missing data, under 5%, were handled by multiple imputation. Sample size calculation, based on prior pilots assuming 25% progression rate, ensured 85% power to detect a hazard ratio of 1.8 for poor PSQI scores.

Results

The 320 participants had a mean age of 58.4 ± 9.2 years, with 50.6% male and a mean systolic blood pressure of 152 ± 14 mmHg despite multidrug therapy. Mean PSQI score was 8.7 ± 3.4, indicating generally poor sleep quality, while actigraphy showed average sleep efficiency of 78% ± 11%. Over the 18-month follow-up from March 2024 to September 2025, 92 patients (28.8%) experienced RH progression, defined by ABPM escalation or treatment intensification. Those with progression had significantly worse baseline sleep metrics (PSQI 10.2 ± 3.1 vs. 7.9 ± 3.2, p<0.001) and higher inflammation markers like hs-CRP (3.2 ± 1.8 vs. 2.1 ± 1.4 mg/L, p=0.002). Multivariable models confirmed sleep as an independent predictor, with consistent patterns across subgroups.

Table 1. Baseline Demographic and Clinical Characteristics of Participants by RH Progression Status

Characteristic	No Progression (n=228)	Progression (n=92)	p-value
Age (years), mean ± SD	57.8 ± 9.0	60.1 ± 9.5	0.012
Male sex, n (%)	112 (49.1)	50 (54.3)	0.378
BMI (kg/m²), mean ± SD	28.4 ± 4.2	29.7 ± 4.8	0.045
Diabetes, n (%)	68 (29.8)	38 (41.3)	0.038
Current smoker, n (%)	42 (18.4)	22 (23.9)	0.267
Baseline SBP (mmHg), mean ± SD	150 ± 13	157 ± 15	<0.001

Table 1 shows key differences between groups, where progressors were older, heavier, and more likely to have diabetes, alongside higher baseline systolic BP. These imbalances, though adjusted in later models, suggest intertwined cardiometabolic risks. Statistical tests revealed moderate effect sizes (Cohen's d ~0.3-0.5), emphasizing the need for covariate control in longitudinal analyses.

Table 2. Baseline Sleep Quality Metrics by RH Progression Status

Metric	No Progression (n=228)	Progression (n=92)	p-value
PSQI total score, mean ± SD	7.9 ± 3.2	10.2 ± 3.1	<0.001
Sleep duration (h), actigraphy	6.8 ± 1.1	6.2 ± 1.3	0.001
Sleep efficiency (%), mean ± SD	81 ± 10	72 ± 11	<0.001
Wake after sleep onset (min)	42 ± 18	58 ± 22	<0.001
Fragmentation index (%)	4.2 ± 1.5	5.8 ± 2.0	<0.001

Sleep metrics starkly diverged, with progressors showing poorer PSQI scores and objective disruptions per actigraphy (all p<0.001, effect sizes d>0.8). These findings point to fragmented, inefficient sleep as a harbinger of RH worsening, independent of demographics in preliminary comparisons, setting the stage for regression modeling (Table 2).

Table 3. Changes in Blood Pressure Metrics Over 18 Months

Time Point	No Progression (n=228)	Progression (n=92)	p-value (interaction)
Baseline 24h SBP (mmHg)	142 ± 12	148 ± 14	-
9 months 24h SBP (mmHg)	138 ± 11	152 ± 15	<0.001
18 months 24h SBP (mmHg)	136 ± 11	158 ± 16	<0.001
Nocturnal dipping (%)	12.5 ± 4.2	8.1 ± 3.8	0.002

ABPM trajectories diverged markedly, with progressors exhibiting non-dipping patterns and steeper SBP rises (group-time interaction F=24.3, p<0.001). This underscores nocturnal hypertension's role, amplified in poor sleepers, as evidenced by repeated-measures ANOVA (Table 3).

Table 4. Multivariable Cox Regression for Predictors of RH Progression

Predictor	HR (95% CI)	p-value
PSQI score (per 1-unit increase)	1.18 (1.10-1.26)	<0.001
Sleep efficiency (per 5% decrease)	1.32 (1.20-1.46)	<0.001
Age (per 10 years)	1.25 (1.05-1.49)	0.012
BMI (per 5 kg/m²)	1.22 (1.04-1.43)	0.015
Diabetes (yes vs. no)	1.41 (0.95-2.10)	0.089

After adjusting for confounders, PSQI and sleep efficiency emerged as robust predictors (model c-statistic 0.78), with hazards indicating 18-32% increased risk per unit worsening. Proportional hazards assumption held (p>0.1), affirming sleep's independent prognostic value (Table 4).

Table 5. Biomarker Levels at Baseline and 18 Months by Progression Status

Biomarker	No Progression Baseline	Progression Baseline	p (baseline)	No Prog. 18 mo	Prog. 18 mo	p (change)
hs-CRP (mg/L)	2.1 ± 1.4	3.2 ± 1.8	0.002	2.0 ± 1.3	4.1 ± 2.2	<0.001
Aldosterone-renin ratio	25 ± 12	32 ± 15	0.008	24 ± 11	38 ± 18	0.001

Inflammation and neurohormonal activation intensified in progressors, with hs-CRP rising disproportionately (paired t-test t=5.6, p<0.001). Baseline elevations correlated with poor sleep (r=0.42, p<0.001), suggesting mechanistic links (Table 5).

Table 6. Kaplan-Meier Estimates of RH Progression-Free Survival

Time (months)	No Progression Group (%)	Progression Group (%)	Log-rank p
6	98.2	89.1	-
12	92.1	68.5	<0.001
18	85.5	41.3	<0.001

Survival curves separated early, with poor sleepers facing 2.1-fold higher progression risk (log-rank χ^2=32.4). This visual divergence highlights sleep's temporal influence on outcomes (Table 2).

Table 7. Subgroup Analysis: HR for PSQI by Age and Sex

Subgroup	n	HR per PSQI unit (95% CI)	p-interaction
Age <60 years	168	1.15 (1.05-1.26)	0.321
Age ≥60 years	152	1.22 (1.11-1.34)	
Male	162	1.20 (1.09-1.32)	0.456
Female	158	1.16 (1.06-1.27)	

Associations held across strata, with slightly stronger effects in older patients and men, though interactions were non-significant, supporting broad applicability (Table 7).

Table 8. PSQI Component Scores Predicting Progression (Multivariable Logistic Regression)

PSQI Component	OR (95% CI) per unit	p-value
Subjective quality	1.45 (1.22-1.73)	<0.001
Sleep disturbances	1.38 (1.18-1.62)	<0.001
Daytime dysfunction	1.29 (1.11-1.50)	0.001
Duration	1.22 (1.04-1.44)	0.016

Specific disturbances like frequent awakenings drove risk (Nagelkerke R^2=0.32), with odds ratios indicating clinical relevance for targeted interventions (Table 8).

Discussion

Our findings reveal a compelling link between poor sleep quality and accelerated resistant hypertension (RH) progression in this Uzbek cohort, where baseline PSQI scores averaging 10.2 in progressors predicted outcomes with an adjusted hazard ratio (HR) of 1.18 per unit increase far surpassing many traditional risks. Actigraphy corroborated this, showing 72% sleep efficiency tied to a 32% higher progression risk per 5% decrement, aligning with global evidence of sleep fragmentation fueling nocturnal hypertension. In Uzbekistan's context, marked by urbanization-driven sleep disruptions, these metrics (all $p<0.001$) highlight how everyday factors amplify RH's toll, explaining why 28.8% progressed despite therapy. Unlike Western studies emphasizing apnea, our PSQI focus uncovered subjective disturbances as key drivers, suggesting broader applicability in resource-limited settings where full polysomnography is rare.

The stark divergence in ABPM trajectories progressors' systolic BP climbing to 158 mmHg by 18 months versus 136 in non-progressors (interaction $p<0.001$) mirrors sleep's role in blunted nocturnal dipping (8.1% vs. 12.5%). This echoes trials like APPLE, but our prospective design over 18 months from 2024-2025 adds temporal depth, with Kaplan-Meier curves separating early (log-rank $p<0.001$). Elevated hs-CRP (3.2 to 4.1 mg/L) in progressors further implicates inflammation, correlating moderately with PSQI ($r=0.42$), a pathway underexplored in Central Asian RH cohorts. These results challenge the notion that RH progression is purely pharmacological, urging sleep integration into risk models (c-statistic 0.78 post-adjustment). Comparisons with international data strengthen our claims: a meta-analysis reported similar HRs (1.15-1.25) for poor sleep in hypertension, yet few address resistance specifically. Our older, heavier progressors (age 60.1 years, BMI 29.7) align with SPRINT subgroups, but subgroup HRs (1.15-1.22) showed consistency across ages and sexes (p-interaction >0.3), countering age-specific biases. Uzbekistan's unique profile rural-urban mix, high diabetes (41.3% in progressors) likely intensified effects, as cultural late evenings compounded short duration (6.2 hours). Still, residual confounding from unmeasured shift work warrants caution, though multivariable adjustments mitigated this.

Mechanistically, our biomarker rises (aldosterone-renin ratio 32 to 38) suggest sleep deficits sustain renin-angiotensin overdrive, exacerbating vascular stiffness a hypothesis bolstered by PSQI components like disturbances (OR 1.38). This resonates with animal models of sleep restriction inducing endothelial dysfunction, tailored here to human RH endpoints. Limitations include reliance on actigraphy over gold-standard polysomnography, potentially underestimating apnea, and modest sample size, though powered adequately (85%). Loss to follow-up was minimal (<5%), enhancing reliability. From a clinical standpoint, these data advocate routine PSQI screening in Uzbek RH clinics, where simple thresholds (e.g., score >9) could flag high-risk cases for behavioral sleep interventions, potentially averting 20-30% of progressions based on our HRs. Public health implications loom large: with Uzbekistan's cardiovascular mortality at 48%, integrating sleep education into national programs could yield cost-effective gains, especially given low intervention barriers.

Our study's strengths prospective tracking at a premier Tashkent center, hybrid subjective-objective sleep measures, and robust statistics (Schoenfeld $p>0.1$) position it as a foundational contribution to Central Asian cardiology. It extends prior work by quantifying progression risks in a novel population, filling a void where local data lagged global trends.

Conclusions

In summary, this 18-month Uzbek cohort study establishes poor sleep quality, quantified by PSQI >10 and efficiency <75%, as a potent independent predictor of RH progression (HR 1.18-1.32), intertwined with inflammation and nocturnal BP surges. With 28.8% progression despite therapy, these metrics outperformed some comorbidities, urging their inclusion in risk stratification to curb cardiovascular burdens in similar settings. Clinically, clinicians should prioritize sleep assessments in RH management, targeting disturbances via hygiene counseling or weight loss, potentially stabilizing trajectories as seen in our ABPM divergences. This low-cost approach suits Uzbekistan's strained system, promising reduced events through early detection. Ultimately, our work underscores sleep's modifiable role in RH, calling for larger trials validating interventions and regional guidelines. By spotlighting Central Asia's overlooked dynamics, it paves the way for holistic strategies, transforming sleep from sidelined factor to frontline ally against hypertension's advance.

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