ANKARA MEDICAL JOURNAL

Vol. 26 / Num. 1, 2026
www.ankaramedj.com
e-ISSN: 2148-4570

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Organization, Preparation and Correspondence
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Date of Issue: 24.03.2026

Ankara Medical Journal is an international peer-reviewed journal and is published quarterly. The responsibility of the published articles belongs to the authors.

Ankara Medical Journal is indexed / abstracted in Scopus, DOAJ, ULAKBIM TR Index, Google Scholar, Index Copernicus, ROAD, ResearchBib, SHERPA/RoMEO, Turkish Citation Index and Turkish Medline.

ANKARA MEDICAL JOURNAL

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Research Article

Ankara Med J, 2026;(1):1-16 // 10.5505/amj.2026.50328

CIRCADIAN BLOOD PRESSURE PHENOTYPES AND 24-HOUR VARIABILITY AS DETERMINANTS OF MENTAL HEALTH-RELATED QUALITY OF LIFE IN HYPERTENSION WITH TYPE 2 DIABETES AND OBESITY

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Submitted: 22.11.2025 // Accepted: 26.02.2026

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ANKARA MEDICAL JOURNAL

Abstract

Objectives: Multimorbidity combining hypertension (HTN), type 2 diabetes mellitus (T2D), and obesity adversely affects health-related quality of life (HRQoL). Ambulatory circadian phenotypes (dipper/non-dipper/riser) and average real variability (ARV) may relate to mental well-being. We aimed to find whether ambulatory BP phenotypes and ARV are associated with the SF-36 mental component summary (MCS) in HTN+T2D+obesity.

Materials and Methods: In an observational cohort, 314 participants with HTN+T2D+obesity (mean age 58.9±9.7 years; 54% men), 262 had evaluable ambulatory blood pressure monitoring (ABPM) (dipper 34%, non-dipper 50%, riser 16%); completed the 36-Item Short-Form Health Survey (SF-36) and underwent 24-hour ambulatory BP monitoring (ABPM). The primary outcome was MCS. 24-h systolic ARV was computed from consecutive valid readings. Receiver-operating characteristic (ROC) analyses identified an ARV threshold for low MCS (the lowest quartile).

Results: Adjusted MCS showed a graded decrement across phenotypes: dipper 48.8 (95% CI 47.5–50.1), non-dipper 46.1 (45.1–47.2), riser 44.0 (42.5–45.6); $p<0.001$. ARV was independently and inversely associated with MCS; for low MCS, ARV discriminated better than SD and mean 24-h SBP (AUC 0.69 vs 0.63 and 0.58). The Youden-derived ARV cut-off ~12.5 mmHg yielded a sensitivity of 0.66 and specificity of 0.62. Simultaneous attainment of 24-h BP and HbA1c targets related to higher MCS (+3.1 points; $p<0.001$) and a greater high-MCS responder rate (52% vs 31%).

Conclusion: In HTN+T2D+obesity, abnormal circadian BP phenotypes and higher ARV identify patients with lower MCS beyond mean BP and may flag risk of low mental HRQoL and support integrated management toward dual control of 24-h BP and HbA1c.

Keywords: Blood pressure monitoring, hypertension, diabetes mellitus, obesity, quality of life, circadian rhythm.

Introduction

Hypertension (HTN), type 2 diabetes (T2D), and obesity frequently co-occur and define a high-risk cardiometabolic phenotype encountered across primary and speciality care. While clinical management understandably prioritises "hard" outcomes (cardiovascular and renal events), patient-reported health-related quality of life (HRQoL) is a key determinant of adherence, self-management, and care utilisation. Generic instruments such as the 36-Item Short-Form Health Survey (SF-36) summarise eight domains into physical (PCS) and mental component scores (MCS), enabling cross-condition comparisons and clinically meaningful change thresholds. Recent work underscores that comorbidity burden—not simply the presence of T2D alone—drives HRQoL loss; for example, patients with T2D plus hypertension show lower SF-36 scores than those with T2D alone, with notable decrements in general health, whereas bodily pain was least affected.[1]

Determinants of HRQoL in T2D are multifactorial and include sociodemographic factors, adiposity, glycemic control, complications, and multimorbidity. In a multicenter study, higher BMI, longer diabetes duration, combined pharmacotherapy, and the presence of complications and comorbidities were each associated with lower PCS and/or MCS, highlighting targets for integrated management beyond glucose alone.[2]

Complementary evidence from primary care shows that systemic arterial hypertension nearly doubles the odds of poor SF-36 HRQoL among people with T2D, and that physical inactivity compounds risk—practical levers for routine care.[3]

Taken together, contemporary data position HRQoL as a clinically salient outcome in the multimorbid cardiometabolic phenotype.

Beyond static clinic blood pressure, ambulatory blood pressure monitoring (ABPM) provides circadian phenotypes (dipper/non-dipper/riser) and beat-to-beat/read-to-reading variability metrics such as average real variability (ARV). These features refine cardiovascular risk stratification; however, their relationship to patient-perceived well-being is understudied, particularly in individuals simultaneously living with HTN, T2D, and obesity. This gap is clinically important: non-dipping and "riser" profiles may reflect nocturnal sympathetic activation, sleep disruption, and autonomic dysregulation, all of which plausibly degrade energy, mood, and social functioning—domains central to the SF-36 MCS. Moreover, variability measures like ARV capture short-term hemodynamic lability that patients may experience as instability, palpitations, or fatigue—symptoms that can undermine daily participation and mental health. Yet few studies have examined whether these ABPM signatures add explanatory value for HRQoL beyond mean blood pressure and conventional metabolic covariates.

Parallel lines of evidence suggest that interventions which jointly improve metabolic control and hemodynamics can improve HRQoL. In severe obesity with T2D, 12-month outcomes after laparoscopic sleeve gastrectomy show significant gains in SF-36 PCS overall, with MCS improvements linked to remission and better metabolic indices—supporting the broader concept that integrated risk-factor control can translate into perceived well-being.[4]

Against this backdrop, routine assessment of HRQoL has been advocated as part of longitudinal diabetes care to inform tailored interventions.[1]

The primary study objective was to test whether circadian ABPM phenotypes (dipper/non-dipper/riser) and 24-h systolic BP ARV are independently associated with SF-36 MCS in patients with coexisting HTN, T2D, and obesity. Secondary objectives were to compare MCS across phenotypes and to assess whether "dual control" (24-h BP and HbA1c at target) is associated with higher MCS.

Materials and Methods

Study design and population

We conducted an observational study of consecutive adults with established HTN and T2D followed in a cardiometabolic clinic.

Inclusion criteria: age ≥18 years; body mass index (BMI) ≥30 kg/m^2; established HTN and T2D; completion of the SF-36 questionnaire within ±2 weeks of ABPM; and availability of a valid 24-h ABPM recording within the previous 4 weeks.

Exclusion criteria: secondary hypertension; symptomatic heart failure, NYHA III–IV; recent acute coronary syndrome or stroke (<3 months); advanced CKD (stage 4–5; eGFR <30 mL/min/1.73 m^2); active inflammatory/autoimmune disease; pregnancy; or inability to complete questionnaires.

Rationale for key exclusions: We excluded NYHA III–IV heart failure and CKD stage 4–5 (eGFR <30) because advanced HF/CKD may markedly affect both ambulatory BP phenotypes/variability and HRQoL and could compromise ABPM feasibility/quality. Dose adjustments of routine therapies in patients with reduced eGFR (e.g., <60) were performed according to standard clinical practice and were not used as eligibility criteria. Current medications were recorded from medical records and participant reports at the study visit and grouped by drug class (RAS blockers, diuretics, calcium-channel blockers, beta-blockers, and antidepressant/anxiolytic/sedative drugs).

The protocol complied with the Declaration of Helsinki and was approved by the institutional bioethics committee (The Bioethics Committee of Kharkiv National Medical University, Kharkiv, Ukraine; protocol №3, 03.11.2021). All participants provided written informed consent before any study procedures.

Ambulatory blood pressure monitoring and phenotypes

ABPM was performed on a routine clinic day using a validated oscillometric device. Cuff size was selected per arm circumference. Measurements were scheduled every 20–30 minutes during daytime and every 30–60 minutes during nighttime; recordings with <70% valid readings, daytime <14 h or nighttime <6 h were repeated. Mean 24-h, daytime, and nighttime systolic/diastolic BP were computed using diary-defined sleep/wake periods (daytime = awake; nighttime = asleep), with manual editing when needed. Nocturnal SBP fall (%) was calculated as (daytime SBP − nighttime SBP) / daytime SBP ×100.

Circadian phenotypes were defined a priori as: dipper (10–20%), non-dipper (<10%), riser (≤0% dip), and extreme dipper (>20%). Twenty-four-hour BP variability was summarised by the ARV of SBP, computed as the mean of absolute differences between consecutive valid readings over 24 h; 24-h SD of SBP was also derived for sensitivity analyses.

The ARV of 24-h SBP was calculated according to the formula from Mena et al.[5] At the ABPM visit, we recorded age, sex, BMI, smoking status, diabetes duration, and clinic BP. Fasting blood samples within ±4 weeks provided HbA1c, lipid profile, creatinine (for eGFR using CKD-EPI), and high-sensitivity C-reactive protein (optional). Achievement of guideline targets was defined before analysis as 24-h BP control (<130/80 mmHg on the 24-h profile) and glycaemic control (HbA1c ≤7.0%); "dual control" indicated meeting both thresholds. Use of antidepressants/anxiolytics/sedatives was coded (yes/no).

Health-related quality of life (SF-36)

HRQoL was measured with the SF-36 (the validated Ukrainian SF-36 version with norm-based scoring (mean 50, SD 10), consistent across participants). Eight domain scores (0–100, higher is better) were computed per manual and aggregated into PCS and MCS component summary scores using standard algorithms, PCS reflects predominantly Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), and General Health (GH), whereas MCS reflects Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH) (standard SF-36 weighting approach). The primary outcome was MCS; secondary outcomes were VT, RE, SF, MH, and PCS. For cross-sectional risk stratification, we defined a high-MCS threshold as an MCS ≥3 points above the sample median; this label is used only to contrast groups at a single time point and does not imply individual change. In a longitudinal sensitivity analysis among participants who completed a repeat SF-36 at routine

follow-up, the minimal clinically important difference (MCID) was defined a priori as a ≥3-point within-person increase in MCS.

Sample size and power

This observational study used a consecutive sampling approach. A sensitivity analysis using G*Power (one-way ANOVA, three groups, α=0.05, power=0.80) indicated that the available ABPM sample (n=262) was sufficient for the primary comparison of MCS across circadian ABPM phenotypes, corresponding to a small-to-moderate between-group effect.

Statistical analysis

Continuous variables are presented as mean±SD or median (IQR), and categorical variables as counts (%). Between-group comparisons used t-tests/ANOVA or Mann–Whitney/Kruskal–Wallis as appropriate; proportions used χ^2/Fisher tests. Associations of ABPM phenotypes and variability with HRQoL were examined using multivariable linear models with MCS (and domains) as dependent variables and the following prespecified covariates: age, sex, BMI, HbA1c, mean 24-h SBP, diabetes duration, smoking, antidepressant use, and lipid-lowering therapy. Diabetes duration was treated as a continuous covariate in all primary models and was not dichotomised (e.g., <10 vs ≥10 years) to avoid information loss and arbitrary cut-points. To estimate the ability of ARV to identify low MCS (the lowest quartile), we built logistic models and receiver-operating characteristic (ROC) curves; the optimal ARV cut-point was derived by Youden's index with 95% CIs. This Youden-derived threshold was then applied to define a binary high-ARV category for subsequent categorical analyses. We also modelled dual control (24-h BP + HbA1c targets) versus neither/one target using ANCOVA for mean differences in MCS and a binary MCID-responder analysis. Collinearity diagnostics and model assumptions (linearity, homoscedasticity, normality of residuals) were checked. Missing data were minimal; complete-case analysis was used. Two-sided $p<0.05$ was considered statistically significant. Analyses were performed in MedCalc, Belgium.

Results

A total of 314 adults fulfilled eligibility and completed HRQoL assessment; of these, 262 (83.4%) also had evaluable 24-h ABPM recordings and comprised the ABPM analytic set (Table 1). The mean age was 58.9±9.7 years; 54% were men; median diabetes duration was 8.1 (IQR 4.0–14.0) years; and mean BMI was 33.6±4.7 kg/m^2. Antihypertensive therapy included a renin–angiotensin system blocker in 88%, a diuretic in 76%, a calcium-channel blocker in 69%, and a beta-blocker in 42%; 12% reported regular use of antidepressants,

anxiolytics, or sedatives. Among laboratory variables available within ±4 weeks, mean HbA1c was 7.4±1.1%, and mean eGFR 78±19 mL/min/1.73 m^2.

Table 1. Baseline characteristics of the study cohort

Characteristic	Overall (n=314)	ABPM (n=262)	Dipper (n=89)	Non-dipper (n=131)	Riser (n=42)	p-value*
Age, years	58.9 ± 9.7	58.9 ± 9.7	58.4 ± 9.8	59.1 ± 9.5	59.8 ± 9.9	0.183
Male sex, n (%)	170 (54.1)	141 (53.8)	47 (52.8)	68 (51.9)	26 (61.9)	0.410
BMI, kg/m^2	33.6 ± 4.7	33.6 ± 4.7	33.3 ± 4.6	33.7 ± 4.7	34.0 ± 4.9	0.367
Diabetes duration, years	8.1 (4.0–14.0)	8.1 (4.0–14.0)	7.9 (4.0–13.5)	8.2 (4.2–14.1)	8.5 (4.1–14.8)	0.521
HbA1c, %	7.4 ± 1.1	7.4 ± 1.1	7.3 ± 1.1	7.4 ± 1.2	7.6 ± 1.1	0.094
eGFR, mL/min/1.73 m^2	78 ± 19	78 ± 19	79 ± 18	78 ± 19	76 ± 20	0.441
Antidepressants/anxiolytics/ sedatives, n (%)	38 (12.1)	31 (11.8)	8 (9.0)	15 (11.5)	8 (19.0)	0.218
24-h mean SBP / DBP, mmHg	---	132 ± 12 / 78 ± 8	130 ± 11 / 77 ± 7	132 ± 12 / 78 ± 8	136 ± 14 / 79 ± 9	0.020 / 0.211
Daytime SBP / DBP, mmHg	---	136 ± 13 / 81 ± 8	---	---	---	---
Nighttime SBP / DBP, mmHg	---	124 ± 14 / 73 ± 9	---	---	---	---
ARV 24-h SBP, mmHg	---	11.6 ± 3.2	10.4 ± 2.7	11.7 ± 3.0	13.5 ± 3.4	0.001
SD 24-h SBP, mmHg	---	12.9 ± 3.8	12.2 ± 3.5	13.0 ± 3.7	13.9 ± 4.1	0.030
Phenotype distribution, n (%)	---	---	89 (34.0)	131 (50.0)	42 (16.0)	---
24-h BP control <130/80, n (%)	---	120 (46)	44 (49.4)	57 (43.5)	19 (45.2)	0.581
HbA1c ≤7.0%, n (%)	154 (49.0)	129 (48)	46 (51.7)	62 (47.3)	21 (50.0)	0.788
Dual control (both), n (%)	---	89 (34.0)	34 (38.2)	40 (30.5)	15 (35.7)	0.420

BMI, body mass index; HbA1c, glycated haemoglobin; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; ARV, average real variability; SD, standard deviation; ABPM, ambulatory blood pressure monitoring; BP, blood pressure. Data are presented as mean ± standard deviation or number (percentage), as appropriate. Dipper, non-dipper, and riser refer to nocturnal blood pressure patterns based on ABPM measurements. *Significant relationship, p<0.05

Across the ABPM cohort, the 24-h mean systolic/diastolic BP was 132±12 / 78±8 mmHg; daytime 136±13/81±8 mmHg; nighttime 124±14/73±9 mmHg. The distribution of circadian phenotypes was: dipper 34% (n=89), non-dipper 50% (n=131), and riser 16% (n=42); over dippers were not observed. The 24-h ARV of SBP averaged 11.6±3.2 mmHg (range 6.2–20.7), while the 24-h SD of SBP was 12.9±3.8 mmHg. By prespecified clinical thresholds, 24-h BP control (<130/80 mmHg) was achieved in 46%, HbA1c ≤7.0% in 48%, and dual control (both targets) in 34% of participants. In the full HRQoL cohort (n=314), the MCS was 46.9±9.1 and the PCS 46.2±8.7 (norm-based scoring). Among those with ABPM (n=262), adjusted comparisons across circadian phenotypes demonstrated a graded decrement in MCS from dipper to riser (Table 2): 48.8 (95% CI 47.5–50.1) in dippers, 46.1 (45.1–47.2) in non-dippers, and 44.0 (42.5–45.6) in risers (p=0.001). VT, SF, and MH exhibited parallel gradients (all p<0.01), whereas PCS differences were modest and non-significant after adjustment. Domain-level adjusted means are shown in Table 2.

Table 2. SF-36 outcomes by ABPM phenotype (adjusted estimates*)

Outcome	Dipper (n=89)	Non-dipper (n=131)	Riser (n=42)	P**
MCS (adjusted mean, 95% CI)	48.8 (47.5–50.1)	46.1 (45.1–47.2)	44.0 (42.5–45.6)	0.001
VT (adjusted mean)	62	56	52	0.003
SF (adjusted mean)	79	73	69	0.007
MH (adjusted mean)	75	70	66	0.001

ABPM: Ambulatory blood pressure monitoring, MCS: Mental Component Summary; VT: vitality; SF: social functioning; MH: mental health; CI: confidence interval. *Adjusted for age, sex, BMI, HbA1c, mean 24-h SBP, diabetes duration, smoking, antidepressant/anxiolytic/sedative use, and lipid-lowering therapy **Significant relationship, $p < 0.05$

Associations between ABPM features and HRQoL showed that in multivariable linear models (covariates: age, sex, BMI, HbA1c, mean 24-h SBP, diabetes duration, smoking, antidepressant use, lipid-lowering therapy), non-dipper and riser phenotypes were independently associated with lower MCS compared with dipper (overall p<0.001, Table 2). The estimated adjusted mean differences vs dipper were −2.7 points (95% CI −3.8 to −1.2) for non-dippers and −4.8 (−6.7 to −2.9) for risers. Patterns were consistent for VT, SF, and MH (all p<0.01), with smaller and non-significant effects for PCS.

Categorising ARV into tertiles yielded a stepwise risk: compared with T1 (≤9.8 mmHg), T2 (9.9–12.4 mmHg) had aOR 1.42 (95% CI 0.88–2.28; p=0.15), and T3 (≥12.5 mmHg) had aOR 2.12 (1.28–3.52; p=0.003) (Table 3). In multivariable logistic models defining low MCS as the cohort-specific lowest quartile (≤42 points), each 1-

mmHg increase in 24-h SBP ARV was associated with higher odds of low MCS (aOR 1.23; 95% CI 1.08–1.40; p=0.002), independent of mean 24-h SBP and metabolic covariates (Table 3).

Receiver-operating characteristic (ROC) analyses showed that ARV outperformed SD and mean 24-h SBP for identifying low MCS. The area under the curve (AUC) for ARV was 0.69 (95% CI 0.63–0.75), compared with 0.63 (0.57–0.70) for SD and 0.58 (0.52–0.64) for mean 24-h SBP. The Youden-derived ARV threshold was ~12.5 mmHg, yielding a sensitivity of 0.66 and a specificity of 0.62 for low MCS. Performance was similar across sex and BMI strata (interaction p>0.10).

Dual target attainment and clinically meaningful change. In analyses comparing participants with dual control (24-h BP and HbA1c at target) versus those with neither or only one target achieved, adjusted mean MCS was higher by +3.1 points (95% CI +1.5 to +4.6; p<0.001). In a cross-sectional responder framework (high-MCS threshold: MCS ≥3 points above the sample median), the responder rate was 52% with dual control versus 31% otherwise (risk ratio 1.68; 95% CI 1.28–2.19; p<0.001).

Results were robust in sensitivity analyses: excluding participants on antidepressants/anxiolytics/sedatives (n=31) produced nearly identical estimates for phenotype and ARV associations with MCS (all p values within 0.02 of primary). Using fixed clock-time windows for day/night in place of diary-based sleep intervals yielded similar phenotype classification and effect sizes. Additional adjustment for the number of antihypertensive classes and for statin use did not materially alter coefficients. When defining low MCS as the lowest tertile rather than quartile, the ARV AUC was 0.68 (0.62–0.74) and the optimal threshold remained close to 12.5 mmHg. Substituting 24-h SD for ARV attenuated associations and discrimination, consistent with the primary analysis.

There were no adverse events related to ABPM acquisition. Missingness was low (<3% for any single covariate); complete-case analyses were used for models and ROC. The proportion of invalid ABPM recordings on the first attempt was 6.8%; these were repeated per protocol and excluded if repeat quality criteria were not met (final evaluable n=262).

Table 3. ARV and dual control in relation to low MCS (adjusted models*)

Metric	Categories / Predictor	Estimate	95% CI	p
Low MCS (lowest quartile)	**ARV T2 vs T1**	aOR 1.42	0.88–2.28	0.150
	ARV T3 vs T1	aOR 2.12	1.28–3.52	0.003
ROC AUC (low MCS)	**ARV (mmHg)**	0.69	0.63–0.75	#
	24-h SD SBP (mmHg)	0.63	0.57–0.70	---
	Mean 24-h SBP (mmHg)	0.58	0.52–0.64	---
Dual control (24-h BP+HbA1c at target)	ΔMCS (adjusted mean)	+3.1	+1.5 to +4.6	0.001
	High-MCS responders	RR 1.68	1.28–2.19	0.001

MCS: Mental Component Summary; ARV: average real variability; T1–T3: tertiles 1 to 3; aOR: adjusted odds ratio; ROC: receiver operating characteristic; AUC: area under the curve; SD: standard deviation; SBP: systolic blood pressure; BP: blood pressure; HbA1c: glycated hemoglobin; ΔMCS: change in Mental Component Summary score; RR: relative risk; CI: confidence interval. *Models adjusted for age, sex, BMI, HbA1c, mean 24-h SBP, diabetes duration, smoking, antidepressant/anxiolytic/sedative use, and lipid-lowering therapy, as applicable (see Statistical analysis) # – Youden-derived ARV threshold ≈12.5 mmHg; sensitivity 0.66; specificity 0.62

Discussion

This study highlights three clinically actionable messages for managing the multimorbidity phenotype of HTN plus T2D and obesity. The riser phenotype—i.e., absent nocturnal BP fall—was consistently associated with the lowest MCS and the largest drops in VT/SF/MH; non-dippers showed intermediate impairment, while dippers had the most favourable profile.

Circadian BP phenotypes (dipper/non-dipper/riser) and ARV are independently associated with the mental component of health-related quality of life (HRQoL) and with emotion/energy domains (vitality, social functioning, mental health), beyond mean BP and conventional cardiometabolic covariates. Second, an ARV threshold around ~12.5 mmHg pragmatically flags patients at higher risk of low MCS. Third, simultaneous attainment of 24-h BP and HbA1c targets is associated with clinically meaningful (MCID-level) gains in MCS, suggesting that integrated hemodynamic and glycemic control shifts perceived well-being, not only "hard" outcomes.

Interpretation and putative mechanisms. Non-dipping and riser patterns indicate loss of the normal nocturnal BP decline and often reflect autonomic dysregulation, heightened nighttime sympathetic tone, impaired baroreflex control, obstructive sleep apnea, or increased arterial stiffness. Contemporary work underscores that abnormal circadian BP rhythms track with neurocognitive risk and sleep disruption, supporting a pathway whereby nocturnal sympathetic activation and fragmented sleep erode mental health and vitality. [6] ARV captures short-term, successive BP fluctuations across the 24-h cycle; greater lability may be intrinsically "fatiguing," perceived as inner tension, palpitations, non-restorative sleep, and daytime tiredness, which plausibly depresses SF-36 VT/SF/MH and overall MCS.

The observed association between dual target attainment (24-h BP + HbA1c) and better MCS is biologically consistent. Glycemic improvement can lessen nocturia and neuropathic discomfort, improve sleep continuity, and reduce low-grade inflammation; when combined with smoother 24-h hemodynamics, this may reduce somatic arousal and fatigue—key drivers of the mental domains. Recent primary-care and speciality studies show that in multimorbid T2D populations, non-biomedical determinants (pain, inactivity, adherence, social and economic stressors) materially shape HRQoL alongside clinical parameters.[7,8] Our findings fit this multidimensional picture while adding an ambulatory hemodynamic lens (phenotype + variability).

Hypertension and HRQoL. A multi-facility cross-sectional study analysis using WHOQOL-BREF confirmed lower HRQoL among adults with HTN and identified modifiable correlates (physical inactivity, low social support, comorbidity, longer antihypertensive treatment duration) as key levers.[9] These data align with our emphasis on targeted behavioural and system-level supports once high-risk ABPM profiles are identified.

A recent global meta-analysis of 22 studies (n=5,447) confirmed a consistent HRQoL decrement in hypertension on the SF-36—pooled means PCS 60.0 and MCS 60.1, falling after trim-and-fill to 52.3% (PCS) and 46.4% (MCS), with substantial heterogeneity by continent, data-collection mode, and sample size.[10] In our cohort, MCS 46.9 ± 9.1 closely matches the bias-adjusted global MCS, reinforcing the salience of mental HRQoL impairment in treated hypertension. We also demonstrate a graded, confounder-adjusted decline across ambulatory phenotypes (dipper – non-dipper – riser), underscoring circadian BP dysregulation as a determinant of mental well-being. Beyond the meta-analytic scope, non-dipping/riser status and higher 24-h ARV independently track lower MCS and VT/SF/MH and outperform SD and mean 24-h SBP for discriminating low MCS. Despite high between-study heterogeneity, the concordance between our MCS and the bias-adjusted benchmark strengthens the external relevance of our results to European outpatient care.

In a Croatian T2D cohort, Kolarić et al. used WHOQOL-BREF and showed that HRQoL declined across all domains, with the lowest scores in patients with multiple chronic complications and the highest in those without complications.[11] In this study, domain-specific patterns emerged—social functioning was poorest with

retinopathy/neuropathy, while physical functioning was lowest with nephropathy or diabetic foot ulcer—highlighting the cumulative burden of vascular and neuropathic damage. Our multimorbid cohort complements these findings by demonstrating that, beyond structural complication load, circadian BP phenotypes and higher 24-h ARV independently track lower MCS on the SF-36. Notably, our mean MCS sits below the psychological/social WHOQOL-BREF means reported by Kolarić et al., plausibly reflecting instrument scaling, greater clinical complexity, and the added impact of circadian BP dysregulation. Together, these data argue for an integrated approach that screens for diabetes complications while routinely performing ABPM to detect high-variability, non-dipping/rising patterns, thereby targeting patients most likely to benefit from combined cardio-metabolic optimisation and psychosocial support.[11]

Alsaidan et al. surveyed T2D in Saudi primary care using the SF-20 (Arabic) and found HRQoL highest for role functioning but lowest for social functioning and pain, with higher odds of better HRQoL in men and those on oral hypoglycemics, and lower in obese, irregular-follow-up, or comorbid patients.[8] In our HTN+T2D+obesity cohort, mental health–related domains (MCS and VT/SF/MH) are likewise most impaired, and we further show that ABPM phenotypes BP and higher 24-h ARV independently track poorer MCS beyond mean BP and metabolic covariates. Despite different instruments (SF-20 vs SF-36), both studies converge on actionable levers—reinforcing follow-up/adherence and pain management—while our data adds circadian BP dysregulation as a modifiable correlate.

In a Romanian T2D cohort with inadequate glycemic control, age and BMI were inversely associated with diabetes-specific QoL (ADDQoL), while SF-36 domains showed minimal associations and no link with HbA1c.[7] Echoing this, our data suggest that mental HRQoL is driven less by glycemia per se and more by hemodynamic features—non-dipping/riser status and higher 24-h ARV—independent of age and BMI. In a cross-sectional study in Mexico, 80% of patients had SF-36 > 50, but physical inactivity (OR 2.76), hypertension (OR 1.93), and female gender (OR 2.82) independently increased the odds of low HRQoL (SF-36 ≤ 50). A higher percentage of body fat was associated with lower SF-36 total and domain scores (especially for physical function, vitality, and mental health), while no association was found with HbA1c.[3] A 2025 public-health study showed graded HRQoL loss from T2D alone to T2D with comorbidities, with the largest decrement in T2D+ cancer, followed by thyroid disease, while hypertension and kidney disease were associated with modest reductions.[1] Together, these reinforce that co-occurring HTN meaningfully worsens the HRQoL profile in T2D—consistent with our observation that non-dipping/riser and higher ARV map most strongly to mental/energy domains.

Among Indonesian adults with hypertension, counselling-intensive care was associated with greater gains in EQ-5D-5L utility over 3 months versus usual care; moreover, patients attending blood-pressure checks twice monthly had higher utility values than those attending monthly (0.85 vs 0.74), suggesting that structured counselling and more frequent monitoring can translate into measurable HRQoL benefits.[12] In T2D, 3 months'

use of a digital self-management program improved RAND-36 role-physical, role-emotional and emotional well-being, but no between-group differences were seen in other domains, and effects were not sustained at 6 months.[13] Structured counselling and self-management interventions have been associated with improvements in patient-reported outcomes in cardiometabolic settings. [12,13] These findings support our practical suggestion to triage patients with ARV ≥ ~12.5 mmHg or non-dipping/riser into brief, protocolized psycho-behavioural support (education, graded activity, sleep hygiene, medication-taking support, family involvement).

In Afghanistan, more than half of adults receiving care for hypertension screened positive for depressive symptoms, and depression was independently associated with poor blood-pressure control, along with low education, low income, physical inactivity, and comorbidity.[14] Complementing this, in Afghan adults with T2D, hypertension was common (~55%), and depressive symptoms were associated with ≈3-fold higher odds of coexisting hypertension, reinforcing the tight coupling between mood disturbance and BP dysregulation.[15]

These data reinforce the bidirectional linkage between mood and hemodynamic control and help explain why patients with greater ambulatory BP instability often report worse mental HRQoL. This triangulates with our finding that circadian BP type sits close to MCS.

Abnormal BP rhythms and variability are established predictors of adverse “hard” outcomes; showing that these same ambulatory signatures align with the mental domains of HRQoL strengthens the case for routine ABPM not only to refine cardiovascular risk but also to surface hidden psychosocial burden that standard clinic BP may miss.[6]

In a comparative study of hypertensive outpatients (WHOQOL-BREF), costs of care (direct/indirect/total) inversely tracked HRQoL, and multivariable models highlighted income, complication burden, physical activity, smoking, and urban residence as key correlates—underscoring the need for cost-mitigation and integrated behavioural support in hypertension care.[16]

Complementing our results, Guidotti et al.[17] found in hypertensive outpatients that lower SF-36 Vitality was associated with greater psychological distress (SCL-90-R GSI), with Social Functioning partially mediating this link. This dovetails with our observation that VT, SF, and MCS cluster with ambulatory BP instability, reinforcing the case for interventions that boost energy and structured social engagement—particularly in non-dippers/risers. Practically, routine screening for low VT and impaired SF can flag patients most likely to benefit from integrated psycho-behavioural support alongside phenotype-guided BP therapy.

Measure HRQoL routinely. For HTN + T2D + obesity, capture SF-36 (or SF-12) at baseline and follow-up; track MCS and the VT/SF/MH triad specifically, as these are sensitive to pain, inactivity, adherence and social

constraints.[7,8] ABPM yields circadian status (dipper/non-dipper/riser) and ARV—both informative for organ-risk and mental HRQoL risk. Adopt a simple ARV alert. Treat ARV ≥ ~12.5 mmHg as a pragmatic flag for a likely mental-energy burden, triggering a short, structured psychosocial package (tailored education, activity nudges, sleep hygiene, pain management, family engagement) and screening for OSA where appropriate. Aim for dual targets. Manage to both 24-h BP and HbA1c targets, with regular feedback. Our data suggest that dual control is associated with MCID-sized improvements in MCS. Digital self-management and structured exercise programs can help sustain gains.[13] Tailor therapy by ABPM phenotype. In non-dippers/risers, consider chronotherapy, optimise long-acting combinations, and systematically evaluate for OSA; monitor pain and sleep, which strongly influence VT/SF/MH. Address social determinants. Costs, activity habits, and complication load explain a substantial share of HRQoL variance in HTN; integrating social and behavioural support is therefore not optional.[14] In practice, riser or non-dipper status and/or ARV ≥12.5 mmHg should prompt OSA screening, review of 24-h antihypertensive coverage (long-acting combinations, possible evening dosing/chronotherapy), and brief psycho-behavioural support, while pursuing dual control of 24-h BP and HbA1c.

Limitations. Key strengths of the study include using ARV to capture short-term 24-h variability beyond mean BP; multivariable analyses adjusting for metabolic and treatment covariates; and an MCID-anchored responder analysis for MCS, which improves clinical interpretability. Limitations include an observational, single-centre design (precluding causal inference and potentially limiting generalizability) and the absence of dedicated anxiety/depression scales—we used SF-36 VT/SF/MH as validated proxies. Even though multiple recent studies consistently document the adverse impact of HTN and comorbidity burden on HRQoL,[1, 11, 16] these findings warrant confirmation in larger, multicenter cohorts. Finally, we did not model response shift—changes in internal standards or valuation of health states over time—which can bias apparent change in HRQoL; hypertension studies suggest this phenomenon can differentially affect physical vs mental components and warrants attention in longitudinal designs.[7, 10]

We did not prespecify a universal ARV cut-off; the 12.5 mmHg value was cohort-derived for low MCS discrimination and may vary across settings, underscoring the need for further multicenter studies to validate the generalizability of these findings.

Conclusions and perspectives. Test whether lowering ARV through combined strategies—chronotherapy and long-acting regimens for smoother 24-h coverage plus non-pharmacologic autonomic “quieting” (structured exercise, sleep optimisation, pain management, weight loss, digital maintenance)—yields incremental MCS benefits beyond those from mean BP reduction alone. Evidence that task-oriented nursing and exercise programs improve HRQoL in cardiovascular populations makes this testable.[18] Second, evaluate antihypertensive chronotherapy in non-dippers/risers with HRQoL endpoints, integrating OSA work-up. Third,

embed low-intensity maintenance contacts (nurse- or app-delivered), because without maintenance, behavioural effects often wane by 3–6 months; recent trials show that structured follow-up sustains SF-36 gains.[13,18] In parallel, bibliometric mapping indicates accelerating interest in T2D HRQoL measurement and psychosocial correlates, but few studies integrate ambulatory hemodynamic phenotyping—an opportunity our work begins to address.[1]

In adults with hypertension, type 2 diabetes, and obesity, non-dipper/riser circadian phenotypes and greater 24-h BP ARV were independently associated with lower SF-36 MCS, whereas simultaneous attainment of 24-h BP and HbA1c targets was associated with higher MCS. ARV can support risk stratification and triage to integrated care (chronotherapy, long-acting combinations, screening for obstructive sleep apnea, and behavioural support). Prospective studies are warranted to test whether reducing ARV and correcting circadian BP abnormalities improve MCS.

Ethical Considerations: Approval was received from the Ethics Committee of Kharkiv National Medical University, Kharkiv, Ukraine (Protocol No 3, 03.11.2021), and the Principles of the Helsinki Declaration were followed.

Conflict of Interest: The authors declare no conflict of interest.

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