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# Association of allostatic load with health-related quality of life in patients with arterial hypertension: a cross-sectional analysis

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## Summary

AIMS OF THE STUDY: Allostatic load (AL), as a marker of cumulative stress, is associated with higher morbidity and mortality, and reduced health-related quality of life (HrQoL) in healthy adults. In patients with hypertension, AL and its association with HrQoL have not been investigated. Therefore, this study aimed to (1) explore AL in a cohort of hypertensive patients and to (2) determine its association with HrQoL, while controlling for other health-related variables.

METHODS: Cross-sectional data from the Styrian Hypertension Study were analysed and included 126 participants (50% female) with a history of arterial hypertension; the mean age was 60.9 years (standard deviation 9.9). AL was derived from a set of 10 biomarkers including neurophysiological, neuroendocrine, metabolic, cardiovascular and inflammatory parameters. The 36-Item Short Form Health Survey (SF-36) was administered for assessment of HrQoL. Additional health-related variables included sociodemographic data, lifestyle factors and comorbidities.

RESULTS: Calculation of AL resulted in sum scores based on 10 binary variables, which were used to categorise patients as either "low AL" (<3) or "high AL" (≥3). Multivariate adjusted analyses revealed that higher AL was associated with better HrQoL with regard to the mental health domain $F(1,1243) = 7.017$; $p = 0.009$). All other components of HrQoL were not related to AL.

CONCLUSIONS: In contrast to results in healthy populations, we found a positive association between AL and the mental health domain of HrQoL. This finding suggests a specific coping pattern among a subgroup of hypertensive patients, possibly influencing their clinical management and outcome.

***Keywords**: allostatic load, hypertension, mental health, quality of life*

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## Introduction

The concept of allostatic load (AL) refers to the cumulative physiological changes that emerge as a result of constant adaption to a variety of life experiences and stressors [1, 2]. Repeated stress exposure and chronic stress constantly stimulate stress-regulating systems such as the hypothalamic-pituitary-adrenal axis and the autonomic nervous system. Over time, chronic activation of these systems results in their dysregulation and finally leads to aggregate physiological consequences called AL. AL can further lead to allostatic overload and associated adverse health outcomes, such as arterial hypertension, cardiovascular disease, stroke, obesity, diabetes mellitus and depression [3]. Thus, in contrast to homeostasis, allostasis can be interpreted as a model of predictive regulation [4]. It links anticipatory brain activity induced by stressors to psychophysiological and pathophysiological stress responses, such as essential hypertension. "Chronically anticipating a need for higher pressure, the brain mobilizes all low level mechanisms in concert: kidney to retain salt and water, vascular system to tighten, and salt appetite to rise" [4].

Since the introduction of the concept, there have been multiple studies of AL, most of them focusing on older and middle aged adults, working adults or children/adolescents [3]. Although AL is typically derived from a set of neuroendocrine, cardiovascular, immunological and metabolic parameters that are assumed to represent cumulative physiological stress in the organism, there is still no definitive standard way of quantifying it. Nevertheless, the association between AL and health impairment seems to be rather independent of both the individual biomarkers that were included in AL measurement and the type of AL measurement (either Z-score based or with cut points) [5]. Recent work shows that AL could even be operationalised as a multisystem physiological dysregulation with shared variance across biomarkers [6–8]. Most studies focused on healthy adults, and data on AL in patient cohorts are rare

[9–11]. In this context, preliminary results, for example in diabetes mellitus, seem to suggest that findings from AL studies in healthy adults, such as the link between poor self-rated health and high AL [12], may not be transferable to clinical populations, in whom this association was absent [9]. To the best of our knowledge, there are no publications addressing AL and its relations to health measures in patients with arterial hypertension. Whereas in healthy adults higher AL has been linked to lower health-related quality of life (HrQoL), it is not clear if this may also occur in hypertensive patients, in whom HrQoL is known to be diminished compared with normotensive persons [13]. HrQoL plays a crucial role in the clinical management and treatment adherence of these patients [14, 15]. Therefore, it is of interest to explore if AL may be linked to HrQoL in arterial hypertension, thus possibly contributing to the outcome of these patients.

In this study, we investigated AL in a cohort of hypertensive patients and aimed to examine a possible association between AL and HrQoL while controlling for other health-related variables such as sociodemographic and lifestyle factors, as well as for comorbidities that may influence HrQoL.

## Material and methods

### Study population

The current investigation used available cross-sectional data from the Styrian Hypertension Study, a single-centre cohort study that was conducted across 3 years (August 2010 to July 2013) at the Division of Cardiology and Division of Endocrinology and Metabolism, Department of Internal Medicine, Medical University of Graz, Austria [16–19]. The main objective of the study was to evaluate biomarkers in relation to arterial hypertension and cardiovascular risk in hypertensive patients. To briefly summarise, inclusion criteria were a history of arterial hypertension and age 18 years or older. Main exclusion criteria were stroke or myocardial infarction within the previous 4 weeks, pregnancy or lactation in women, and an estimated life expectancy of less than 1 year.

A subgroup of 331 patients were asked to fill in a set of health-related questionnaires: the WHO-Five Well-Being Index (WHO-5), the 36-Item Short Form Health Survey (SF-36), and the International Physical Activity Questionnaire (IPAQ). Additional health-related variables were assessed in the whole study group. Response rates for the questionnaires varied between 62.5% (IPAQ) and 71.6% (WHO-5 and SF-36). For the present analysis we included a subgroup of 126 patients with complete data sets for variables used in AL quantification, WHO-5, SF-36, IPAQ and all other variables. This analysed subgroup did not differ from the other 205 patients in their allostatic load index, sex, age, smoking behaviour, alcohol consumption, body mass index (BMI), physical activity, blood pressure or the presence of diabetes mellitus, cardiovascular disease, previous cancer diagnosis or depressive symptoms (all $p > 0.05$, data not shown).

The Styrian Hypertension Study complied with the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of the Medical University of Graz (IRB00002556). All patients gave written informed consent prior to participation.

### Allostatic load

AL was derived from a set of 10 parameters, comprising heart rate variability, urinary cortisol, total cholesterol, serum high-density lipoprotein (HDL), glycosylated haemoglobin (HbA1c), waist-to-hip ratio, systolic blood pressure (SBP), diastolic blood pressure (DBP), C-reactive protein (CRP) and serum 25-hydroxyvitamin D (25(OH)D). This combination of parameters was chosen to include both primary mediators such as urinary cortisol and heart rate variability and secondary outcomes such as waist-to-hip ratio, HDL and others. We also aimed to cover a broad range of physiological systems by including neurophysiological, neuroendocrine, metabolic, cardiovascular, and inflammatory parameters [3].

For calculating an AL score we applied the original, distribution-based approach [20]. The distribution of each parameter within the sample was assessed and those individuals within the highest risk quartile (usually the highest quartile; the lowest quartile for heart rate variability, HDL and 25(OH)D) were assigned the value “1”, whereas those in the lowest three quartiles were assigned the value “0”. These binary indicators were then summed to give a score (possible range 0–10) with higher values indicating higher physiological strain.

Blood samplings for determination of HbA1c, CRP, total cholesterol, HDL and 25(OH)D were performed in the morning (7:00 to 11:00) after an overnight fast and after 10 minutes in a sitting position. All blood samples were either measured within 4 hours after blood collection or immediately stored at −20°C until analysis.

25(OH)D was measured by means of a chemiluminescence assay (IDS-iSYS 25-hydroxyvitamin $D^S$ assay; Immunodiagnostic Systems Ltd, Boldon, UK) on an IDS-iSYS multidiscipline automated analyser. Results are reported in ng/ml and can be transformed by multiplication by 2.5 into nmol/l. Although serum 25(OH)D is not a common parameter for AL calculation, it has been shown to have a statistically significant association with several measurements of AL and therefore was included in calculating AL [21].

Waist-to-hip ratio was defined as the ratio of the circumference of the waist to that of the hips.

For cortisol measurement, participants collected 24-hour urine samples at the baseline visit. Cortisol was measured with LC-MS/MS using a protocol including derivatisation with PFBHA (0-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine hydrochloride) and MSTFA (methyltrimethylsilyltrifluoracetamide) to cover carbonyl and hydroxyl groups of cortisol. A chromatographic separation was carried out with a HP5-MS column and detection was by means of negative chemical ionisation and a quadrupole mass spectrometer. Quantification was in a range of 1–50 ng/ml, and the coefficient of determination was 0.9909.

Ambulatory blood pressure measurement (ABPM) was used to determine SBP, DBP and heart rate variability. A 24-hour ABPM portable device (SPACELABS 90217A, firmware-version: 03.02.16; Spacelabs Healthcare, Inc., Issaquah, WA) was used and measurements recorded every

15 minutes during the day (6:00–22:00) and every 30 minutes during the night (22:00–6:00). If ambulatory recordings were longer than 24 hours, only the first 24 hours were used for analysis. Mean 24-hour SBP and DBP in mm Hg were calculated as the mean of all valid measurements of systolic and diastolic blood pressure, respectively, during a 24-hour period. Mean 24-hour heart rate variability was defined as the standard deviation of the mean heart rate in the 24-hour ABPM, measured in beats per minute.

### Health-related quality of life

HrQoL was assessed with the 36-Item Short Form Health Survey (SF-36) [22]. The SF-36 is a 36-item multidimensional questionnaire assessing different aspects of health. HrQoL is represented in eight scales (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health). Raw scores were transformed into scales ranging from 0–100, according to the SF-36 user's manual [23].

### Health-related variables

As health-related variables we included available and commonly used health indicators (sociodemographic data, smoking behaviour, alcohol consumption, BMI, physical activity, blood pressure level), as well as additional diagnoses that may be directly or indirectly linked to arterial hypertension and HrQoL (diabetes mellitus, cardiovascular disease, previous cancer diagnosis and a positive screening for depression). All variables were determined via either patient interview or a questionnaire at the baseline visit.

Four age groups were defined: <55 years, 55–60 years, 60–65 years and >65 years.

Smoking behaviour was assessed during patient interview and classified into the categories "never smoked", "previous smoker" and "active smoker".

Alcohol consumption was also ascertained at the interview and grouped into four categories. "Never" applied to strictly abstinent drinking behaviour; "occasionally" was applied when patients reported drinking alcohol less than once per week. If a patient reported a certain weekly amount of alcoholic beverage other than daily, the frequency was considered "regularly". Finally, alcohol consumption four or more times a week was considered "daily" consumption.

BMI was classified as normal (18.5–24.99 kg/m$^2$), overweight (25.0–29.99 kg/m$^2$) and obese (≥30 kg/m$^2$), according to the WHO definition [24].

Physical activity level was determined with the International Physical Activity Questionnaire (IPAQ) [25]. The IPAQ is freely available and was developed as an instrument for cross-national assessment of physical activity and for standardising measures of health-related physical activity behaviours of population in many countries and in different sociocultural contexts. The long self-administered (31-item) version of the IPAQ (revised October 2002) elicits information on physical activity over the "last seven-day" period and has been used to compare physical activity behaviours among and between populations.

Blood pressure level was classified according to ESC 2013 guidelines and manually measured by use of the Korotkoff method at the baseline visit [26].

Diabetes mellitus was determined via patient interview, antidiabetic drug intake, or an HbA1c level ≥6.5% (47.54 mmol/mol) and/or a fasting plasma glucose ≥126 mg/dl (7 mmol/l).

Cardiovascular disease included previous myocardial infarction, stroke / transient ischaemic attack (TIA), other cardiovascular events and/or coronary artery disease.

Previous cancer diagnosis was determined by patient interview.

Finally, increased depressive symptoms were assumed when patients had a score of ≤50 in the WHO-Five Well-Being Index (WHO-5). The WHO-5 is a short and freely available measure for current mental well-being and quality of life [27, 28]. Five items are rated on a six-point scale (0–5), resulting in a raw score of well-being (range 0–25). Raw scores are transformed into percentage scores (range 0–100%) by multiplication by four. A percentage score of 0 represents the worst possible, and a score of 100% the best possible quality of life. A cut-off score of ≤50 can be used to screen for depression, as has been successfully applied in several studies [29].

### Statistical analyses

Statistical analysis was performed with the software PASW Statistics 22 for Windows.

Differences between health-related sample characteristics in the continuous AL-Index were detected with student's t-test for variables with two factor levels (sex, presence of cardiovascular disease, diabetes mellitus, previous cancer or elevated depressive symptoms) or one-way analysis of variance (ANOVA) for variables with three or more factor levels (age, smoking, alcohol consumption, BMI, physical activity and blood pressure level).

Multivariate analysis of covariance (MANCOVA) was used to test for influences of health-related variables on quality of life (SF-36 profiles including the scales physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health). In the case of gender as a fixed factor, MANCOVA was run with adjustment of age as a covariate. To test for the influence of age on SF-36 profiles, MANCOVA included gender as a covariate. MANCOVAs for all other health-related variables possibly influencing HrQoL included both age and sex as covariates.

Finally, another MANCOVA was run to detect influences of AL groups on SF-36 profiles. All health-related variables that had shown significant influences on at least one of the SF-36 scales were included as covariates, namely age, sex, alcohol consumption, BMI, cardiovascular disease, previous cancer and depressive symptoms. Statistical significance was assumed at a p-value of <0.05.

In order to reappraise the counterintuitive results from the final MANCOVA analysis, we decided to estimate the influence of AL and relevant covariates on HrQoL (subdomain mental health) in an additional way, and performed a stepwise multiple linear regression analysis. This procedure would allow detection of a possible artefact that could have emerged as a result of the dichotomisation of AL into high/low instead of using a continuous AL index. In the multiple regression analysis, the mental health domain of the SF-36 served as criterion, predictor variables

were the continuous AL score together with the relevant covariates age, gender, alcohol consumption, BMI, cardiovascular disease, previous cancer, and the WHO-5 percentage scores. Collinearity of predictors could be ruled out.

Concerning the requirements for all parametric analyses employed, homogeneity of variances was tested using Levene's test and could be asserted for almost all variables ($p > 0.05$). In variables where homogeneity of variance was not given (differences in the AL index due to sex, diabetes mellitus and blood pressure level, $p < 0.05$) the corresponding unequal variance tests (Welch tests) were interpreted. Normal distribution of continuous variables was tested using Shapiro-Wilk tests for normality, which showed that most variables were not normally distributed within our sample. However, the statistical analyses used have shown to be robust even when the requirements of normally distributed data are not met [30–32].

## Results

### Allostatic load in arterial hypertension

Descriptive data for the variables used in the calculation of AL and the corresponding cut-off values for the highest-risk quartiles are given in table 1.

After summarisation as binary indicators for the highest risk quartiles, the AL index ranged from 0–7 with a mean of 2.51 (standard deviation [SD] 1.6). AL scores of 0–2 were defined as "low AL" and scores of ≥3 as "high AL", as in previous studies [21, 33]. This resulted in 66 patients (52.2%) with low AL and 60 patients with high AL (47.6%).

Table 2 presents health-related characteristics for the total sample and for the groups with high AL and low AL. In addition, mean AL scores are given for all categories of health-related variables.

Health-related variables that were significantly associated with a higher AL score were male sex ($T(101) = -5.723$, $p < 0.001$), age <55 years ($F(3,122) = 2.96$, $p = 0.035$), daily versus occasional or no alcohol consumption ($F(3,122) = 3.221$, $p = 0.025$), obesity versus normal weight or overweight ($F(2,123) = 8.758$, $p < 0.001$) and hypertension grades 1–3 in relation to high normal blood pressure level (Welch's $F(2,27.7) = 9.178$, $p < 0.001$). The only additional diagnosis associated with higher AL was diabetes mellitus ($T(49) = -3.757$, $p < 0.001$).

### Association between allostatic load and HrQoL

To answer the main study question, we analysed the influence of AL groups on HrQoL (table 3). After we had controlled for all health-related variables with significant influences ($p < 0.05$) on at least one subscale of the SF-36 (age, sex, alcohol consumption, BMI, cardiovascular disease, previous cancer and elevated depressive symptoms; data not shown), AL had a significant impact on mental health: among patients with hypertension, those with higher AL reported better mental health ($F(1,1243) = 7.017$, $p = 0.009$).

In order to control for this result a second approach was used to estimate the relationship between AL and HrQoL: we conducted a stepwise multiple linear regression analysis with the mental health domain of the SF-36 serving as criterion. Predictor variables were the continuous AL score as well as the relevant covariates age, gender, alcohol consumption, BMI, cardiovascular disease, previous cancer, and WHO-5 percentage scores.

Results of the stepwise multiple linear regression analysis are presented in table 4 and included the WHO-5 score and AL score as relevant predictors in the models. In model 1 ($F(1,125) = 60.825$, $p < 0.001$) depressive symptoms alone could explain 33% ($R^2 = 0.33$) of variance of the mental health domain. In model 2 ($F(2,125) = 35.643$, $p < 0.001$), AL was included as a second relevant predictor and accounted for an additional 4% of explained variance, resulting in 37% overall ($R^2 = 0.37$) of explained variance of HrQoL in mental health. The predictors age, gender, alcohol consumption, BMI, cardiovascular disease and previous cancer did not explain additional variance and were excluded from the models.

## Discussion

### Allostatic load in arterial hypertension

In the first part of this study we report on AL and its relations to several health-related variables in a clinical sample of hypertensive patients. In general, the relationships between health-related variables and AL that we found in this patient cohort paralleled those in a healthy population. Higher AL was reported for males in other studies also, and higher alcohol consumption has been related to higher AL before [3, 34]. Of course higher BMI, higher blood pressure and diabetes mellitus, which are components of the AL index, were also related to higher AL. However, we found high AL to be associated with younger patients

**Table 1:** Parameters used for calculation of allostatic load.

| | Mean | Standard deviation | Range | Cut-off |
|---|---|---|---|---|
| Waist-to-hip ratio | 0.97 | 0.08 | 0.07–1.12 | >1.04 |
| 24-h SBP (mm Hg) | 127 | 13 | 91–158 | >134 |
| 24-h DBP (mm Hg) | 76 | 9 | 55–104 | >82 |
| 24-h heart rate variability (beats/minute) | 9.9 | 3.4 | 3.3–19.7 | <7.8 |
| HbA1c in plasma (%) | 6.0 | 0.9 | 4.9–9.5 | >6.2 |
| C-reactive protein in plasma (mg/l) | 2.8 | 3.3 | 0.6–22.4 | >3.2 |
| Total cholesterol in plasma (mg/dl) | 200 | 54 | 101–571 | >228 |
| High-density lipoprotein in plasma (mg/dl) | 61 | 18 | 24–120 | <49 |
| 24-h cortisol in urine (µg/24h) | 17.5 | 11.4 | 2.8–78.8 | >23.7 |
| 25-hydroxyvitamin D in serum (ng/ml) | 26.4 | 10.6 | 11.7–73.4 | <19.5 |

SBP = systolic blood pressure; DBP = diastolic blood pressure; HbA1c = glycosylated haemoglobin

in our sample, contradicting what had been shown in non-clinical or mixed samples [3, 11]. This might be due to the fact that, unlike the other age groups assessed, most patients aged <55 years are still working and thus exposed to more daily stress, which could be reflected in higher AL scores. However, we cannot base this assumption on corresponding questionnaire data on current working status, thus possibly limiting validity of results.

**Association between allosteric load and HrQoL**

In contrast to findings in healthy populations, no negative association between AL and HrQoL was revealed in this study among hypertensive patients. On the contrary, we found a positive link between AL and the mental health domain of HrQoL, and all other components of HrQoL were found to be unrelated to AL. In order to further explore this association, multiple regression analysis was conducted. Depressive symptoms were found to be the best predictor for a worse HrQoL in mental health. In addition to depressive symptoms, only AL contributed significantly to the prediction of this aspect of HrQoL and thus substantiated our main finding of an association between high AL and better mental health among hypertensive patients. In other studies, for example in an elderly population, higher AL was associated with worse self-rated health and worse performance in activities of daily life, as well as with depressive symptoms and cognitive impairment [35, 36]. In addition, Nobel et al. did not find any association between AL and mental health as measured with the Mental Component Summary of the SF-12, the short form of the SF-36 [11].

It should be kept in mind that our subgroup with low AL – as compared with healthy samples – probably represents a group with higher physiological strain and our subgroup with high AL virtually constitutes the "tip of the iceberg". Surprisingly, those hypertensive patients with the highest AL – within a group with high physiological stress levels anyway – reported being in a comparably good mood, with low levels of depressive symptoms or anxiety according to the SF-36. How can this association be interpreted? At least two alternatives can be considered. First, it could be assumed that there is a group of hypertensive patients with few comorbidities yet, who might somehow disregard or repress the diagnosis and its consequences, thus enjoying life in a psychologically less burdened way. High AL may be accompanying such a lifestyle of denying health threats. A similar observation was already described for hypertensive patients who did not know yet about their diagnosis. Apparently, it is very much the knowledge of being hypertensive that reduces quality of life in this group [37]. Be-

**Table 2:** Health-related sample characteristics (n = 126) by allostatic load (AL) group, and the continuous AL score.

| | | Total n (%) | AL low n (%) | AL high n (%) | AL score (SD) |
|---|---|---|---|---|---|
| Sex* | Male | 63 (50.0) | 22 (34.9) | 41 (65.1) | 3.24 (1.7) |
| | Female | 63 (50.0) | 44 (69.8) | 19 (30.2) | 1.78 (1.0) |
| Age* in years | <55 | 29 (23.0) | 12 (41.4) | 17 (58.6) | 3.14 (1.7) |
| | 55–60 | 23 (18.3) | 12 (52.2) | 11 (47.8) | 2.35 (1.5) |
| | 60–65 | 29 (23.0) | 13 (44.8) | 16 (55.2) | 2.69 (1.7) |
| | >65 | 45 (35.7) | 29 (64.4) | 16 (35.6) | 2.07 (1.4) |
| | mean (SD) | 60.9 (9.9) | 62.4 (9.3) | 59.3 (10.5) | |
| Smoking behaviour | Never smoked | 64 (50.8) | 34 (53.1) | 30 (46.9) | 2.33 (1.5) |
| | Previous smoker | 52 (41.3) | 28 (53.8) | 24 (46.2) | 2.56 (1.7) |
| | Active smoker | 10 (7.9) | 4 (40) | 6 (60) | 2.90 (1.8) |
| Alcohol consumption* | Never | 25 (19.8) | 19 (76.0) | 6 (26.0) | 1.96 (1.5) |
| | Occasionally | 73 (57.9) | 38 (52.1) | 35 (47.9) | 2.44 (1.6) |
| | Regularly | 15 (11.9) | 6 (40.0) | 9 (60.0) | 2.87 (1.7) |
| | Daily | 13 (10.3) | 3 (23.1) | 10 (76.9) | 3.54 (1.3) |
| BMI* | Normal | 26 (20.6) | 18 (69.2) | 8 (30.8) | 1.81 (1.4) |
| | Overweight | 50 (39.7) | 31 (62.0) | 19 (38.0) | 2.20 (1.4) |
| | Obese | 50 (39.7) | 17 (34.0) | 33 (66.0) | 3.18 (1.7) |
| | Mean (SD), kg/m$^2$ | 29.2 (5.4) | 27.8 (4.5) | 30.7 (6.0) | |
| Physical activity (IPAQ) | Low/light | 12 (9.5) | 7 (58.3) | 5 (41.7) | 2.92 (1.9) |
| | Moderate | 30 (23.8) | 17 (56.7) | 13 (43.3) | 2.30 (1.4) |
| | High/vigorous | 84 (66.7) | 42 (50.0) | 42 (50.0) | 2.52 (1.6) |
| Blood pressure* level | Optimal | 6 (4.8) | 4 (66.7) | 2 (33.3) | 2.17 (1.2) |
| | High normal | 13 (10.3) | 13 (100) | 0 (0) | 1.08 (0.8) |
| | Grade 1 hypertension | 20 (15.9) | 9 (45.0) | 11 (55.0) | 2.80 (2.0) |
| | Grade 2 hypertension | 50 (39.7) | 24 (48.0) | 26 (52.0) | 2.44 (1.3) |
| | Grade 3 hypertension | 36 (28.6) | 15 (41.7) | 21 (58.3) | 3.03 (1.8) |
| Diabetes mellitus* | Yes | 35 (27.8) | 11 (31.4) | 24 (68.6) | 3.43 (1.8) |
| | No | 91 (72.2) | 55 (60.4) | 36 (39.6) | 2.15 (1.4) |
| Cardiovascular disease | Yes | 33 (26.2) | 17 (51.5) | 16 (48.5) | 2.27 (1.4) |
| | No | 93 (73.8) | 49 (52.7) | 44 (47.3) | 2.59 (1.7) |
| Previous cancer diagnosis | Yes | 19 (15.1) | 9 (47.4) | 10 (52.6) | 2.32 (1.1) |
| | No | 107 (84.9) | 57 (53.3) | 50 (46.7) | 2.54 (1.7) |
| Depressive symptoms (WHO-5 screening) | Yes | 28 (22.2) | 14 (50.0) | 14 (50.0) | 2.32 (1.4) |
| | No | 98 (77.8) | 52 (53.1) | 46 (46.9) | 2.56 (1.7) |

AL = allostatic load; BMI = body mass index; SD = standard deviation * For these variables significant group differences were found regarding the AL score

sides, it has been reported that worse interoceptive perception in some patient groups is related to better quality of life. Janssens and Harver, for example, reported that asthma education in children increased their trigger perception but simultaneously reduced quality of life [38]. In addition, the negative association between body weight and quality of life among adolescents is modified by their weight perception: inaccurate weight perception among overweight adolescents makes them perceive higher quality of life than overweight adolescents with accurate weight perception [39]. Or second, the described link between high AL and positive mental health as a HrQoL component could simply reflect a high physiological stress pattern in support of an active and psychologically rewarding lifestyle without any substantial health-related denial.

However, when interpreting the association between high AL and better mental health, we cannot rule out that further variables that have not been assessed in this study (such as personality or socioeconomic status) might have impacted self-rated mental health.

### Strengths and limitations

This is the first study to both assess AL in a clinical sample of hypertensive patients and relate this concept to these patients' quality of life.

One of the limitations of this study relates to the measurement of AL in general. Up to now, there is no gold standard for calculation of AL and multiple sets of variables as well as calculation methods have been applied [12, 34, 40, 41]. However, in a current study Frei et al. found comparable results for the most common methods, using both quartiles and pre-defined cut-off scores [21]. In our study we used parameters from different physiological systems as suggested by Mauss et al. [3] and also included 25(OH)D, which has been shown to be suitable for AL measurement [21]. Another limitation refers to the measurement of AL in this clinical population because the influence of medication on physiology and therefore on the formation of AL groups was not taken into account.

In addition, it is possible that a larger sample size would have revealed further relations between AL and HrQoL. As has been reported recently, such relationships between AL and psychosocial resources are typically small and may need large samples to reach statistical significance [42]. Besides, we cannot compare our findings with a control group, thus also limiting interpretability of results.

Finally, for the discussion of results one should consider the reduced transferability of results from the general population to a clinical population and vice versa [9].

**Table 3:** MANCOVA presenting the influence of allostatic load on health-related quality of life.

| SF-36 scales | AL | Mean | SD | F | p-value |
|---|---|---|---|---|---|
| Physical Functioning | Low AL | 76.05 | 20.65 | 0.248 | 0.620 |
| | High AL | 78.52 | 20.68 | | |
| | Total | 77.23 | 20.62 | | |
| Role physical | Low AL | 51.14 | 45.24 | 3.737 | 0.056 |
| | High AL | 68.05 | 42.83 | | |
| | Total | 59.19 | 44.75 | | |
| Bodily pain | Low AL | 64.06 | 22.69 | 2.571 | 0.112 |
| | High AL | 71.45 | 24.06 | | |
| | Total | 67.58 | 23.55 | | |
| General health | Low AL | 64.77 | 17.76 | 0.016 | 0.900 |
| | High AL | 65.50 | 19.08 | | |
| | Total | 65.12 | 18.34 | | |
| Vitality | Low AL | 57.12 | 17.30 | 3.847 | 0.052 |
| | High AL | 62.67 | 17.15 | | |
| | Total | 59.76 | 17.39 | | |
| Social functioning | Low AL | 76.70 | 24.41 | 1.156 | 0.284 |
| | High AL | 81.46 | 20.49 | | |
| | Total | 78.97 | 22.66 | | |
| Role emotional | Low AL | 82.32 | 36.62 | 0.017 | 0.897 |
| | High AL | 80.00 | 37.93 | | |
| | Total | 81.22 | 37.12 | | |
| Mental health | Low AL | 65.88 | 17.77 | 7.017 | 0.009** |
| | High AL | 73.70 | 14.72 | | |
| | Total | 69.60 | 16.79 | | |

Multivariate analysis: F = 1.997, p = 0.053 Results adjusted for covariates age, sex, alcohol consumption, body mass index, cardiovascular disease, previous cancer and depressive symptoms

**Table 4:** Multiple linear regression analyses of the influence of allostatic load and relevant covariates on the mental health domain of health-related quality of life.

| Model | Included predictors | B | SE B | Beta (β) | t | p-value | 95% CI | $R^2$ | $\Delta R^2$ |
|---|---|---|---|---|---|---|---|---|---|
| 1† | WHO-5 | 0.51 | 0.07 | 0.57 | 7.80 | <0.001 | 0.38–0.64 | 0.33 | 0.33 |
| 2‡ | WHO-5 | 0.49 | 0.06 | 0.55 | 7.60 | <0.001 | 0.36–0.61 | 0.37 | 0.04 |
| | AL | 2.05 | 0.76 | 0.20 | 2.71 | 0.008 | 0.55–3.55 | | |

B = regression coefficient, SE B = standard error, Beta = standardised coefficient † Excluded predictors allostatic load, age, gender, alcohol consumption, body mass index, cardiovascular disease, previous cancer ‡ Excluded predictors age, gender, alcohol consumption, body mass index, cardiovascular disease, previous cancer

## Conclusions

This study revealed that depressive symptoms among hypertensive patients significantly contributed to worse HrQoL in the mental health domain. It suggests that higher AL could be related to better mental health in hypertensive patients. Further research is needed to replicate this result and investigate its clinical implications. If confirmed by other research, this finding may contribute to a more comprehensive and differentiated picture of the role of stress patterns and coping mechanisms in hypertensive patients. A subgroup of hypertensive patients may appear to be emotionally stable, but might be at high physiological risk. Thus, this subgroup may pose specific challenges for patient education as part of clinical management. Further research is needed to confirm these assumptions.

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**Potential competing interests**

The authors have no competing interests to report.

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