

ASSOCIATION BETWEEN CHRONIC STRESS, CORTISOL LEVELS, AND UNCONTROLLED HYPERTENSION CROSS-SECTIONAL ANALYTICAL STUDY

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Abstract

Background: Hypertension remains a major contributor to cardiovascular morbidity worldwide, and achieving adequate blood pressure control remains challenging in many patients despite available treatment options. Increasing evidence suggests that chronic psychological stress and prolonged activation of stress-related biological pathways may influence blood pressure regulation. Cortisol, a key hormone of the hypothalamic-pituitary-adrenal (HPA) axis, may act as an important marker of long-term stress exposure and cardiovascular risk. This study aimed to evaluate the association between chronic stress, cortisol levels, and uncontrolled hypertension among patients attending a tertiary care hospital in Lahore, Pakistan.

Methods: A cross-sectional analytical study was conducted among adult hypertensive patients receiving care at a tertiary care hospital in Lahore. Participants were categorized into controlled and uncontrolled hypertension groups based on their blood pressure status. Demographic and clinical information was collected through a structured questionnaire. Psychological stress was assessed using the Perceived Stress Scale (PSS-10), while serum cortisol levels were measured as a biological indicator of stress response. Blood pressure measurements were obtained using standardized clinical procedures. Statistical analysis was performed to determine associations between stress scores, cortisol levels, and hypertension control status.

Results: A total of 240 hypertensive patients were included, with 120 participants in each group. Patients with uncontrolled hypertension demonstrated significantly higher perceived stress scores compared with controlled hypertensive patients (27.1 ± 5.6 vs. 15.4 ± 4.8 , $p < 0.001$). Serum cortisol levels were also significantly elevated among uncontrolled hypertensive patients (22.6 ± 6.3 $\mu\text{g/dL}$) compared with the controlled group (13.8 ± 4.5 $\mu\text{g/dL}$, $p < 0.001$). Higher stress categories were more frequently observed among patients with uncontrolled blood pressure. A positive association was

observed between psychological stress, cortisol concentration, and elevated blood pressure values.

Conclusion: The findings indicate that chronic stress and increased cortisol levels are significantly associated with uncontrolled hypertension. These results highlight the importance of considering psychological and biological stress factors in routine hypertension management. Incorporating stress assessment and supportive interventions alongside standard antihypertensive therapy may improve blood pressure control and provide a more comprehensive approach to cardiovascular risk reduction.

INTRODUCTION

Hypertension is one of the most common non-communicable diseases and remains a major public health challenge worldwide. It is considered a leading cause of cardiovascular diseases, including stroke, coronary artery disease, heart failure, and kidney complications. Despite the availability of effective antihypertensive medicines, a large number of patients fail to achieve adequate blood pressure control. This problem is more significant in developing countries where limited awareness, poor treatment adherence, lifestyle factors, and psychosocial challenges contribute to uncontrolled hypertension. Pakistan is also facing a growing burden of hypertension due to rapid urbanization, changing lifestyles, dietary patterns, and increasing psychological stress among adults (Jafar et al., 2005).

Blood pressure regulation is influenced by multiple physiological and environmental factors. Traditionally, hypertension has been linked with factors such as age, obesity, excessive salt intake, genetics, and physical inactivity. However, recent evidence suggests that psychological factors, especially chronic stress, may also contribute significantly to poor blood pressure control. Chronic stress is a prolonged psychological condition in which the body remains exposed to repeated emotional or environmental pressures. Unlike short-term stress, which activates protective responses for a limited period, chronic stress may cause continuous stimulation of stress pathways and produce harmful effects on cardiovascular health (Steptoe & Kivimäki, 2012).

The human body responds to stress through two major systems: the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA)

axis. When an individual experiences persistent stress, the HPA axis becomes repeatedly activated, resulting in increased secretion of cortisol from the adrenal glands. Cortisol is an essential hormone involved in metabolism, immune regulation, and adaptation to stress. However, prolonged elevation of cortisol may disturb normal cardiovascular functions by increasing vascular resistance, promoting inflammation, altering glucose metabolism, and affecting endothelial function (McEwen, 2006). These changes may contribute to sustained elevation of blood pressure and difficulty achieving hypertension control.

Several studies have investigated the relationship between cortisol and cardiovascular disease. Cortisol measurement has traditionally been performed through blood, urine, or saliva samples. Recently, hair cortisol concentration has emerged as a useful marker for assessing long-term cortisol exposure because it reflects cortisol secretion over several weeks or months rather than a single moment. Increased hair cortisol levels have been associated with cardiovascular risk factors, including hypertension, obesity, and metabolic abnormalities (Iob & Steptoe, 2019).

Psychological stress may influence blood pressure through both direct and indirect pathways. Directly, stress activates the sympathetic nervous system, increasing heart rate, cardiac output, and vascular tone. Repeated activation of these mechanisms can lead to structural and functional changes in blood vessels, resulting in persistent hypertension. Indirectly, stressed individuals may adopt unhealthy behaviors such as reduced physical activity, poor dietary choices, smoking, disturbed sleep patterns, and medication non-

adherence. These behaviors further increase cardiovascular risk and may contribute to uncontrolled blood pressure (Dimsdale, 2008).

The relationship between stress and hypertension is particularly important in patients already diagnosed with high blood pressure. Although antihypertensive therapy effectively lowers blood pressure in many patients, some individuals continue to have uncontrolled hypertension despite treatment. Psychological stress may be one of the overlooked factors contributing to this treatment failure. Identifying stress-related biological markers such as cortisol may help healthcare providers understand why some patients remain uncontrolled and may support more comprehensive management strategies.

Pakistan presents a unique environment where social, economic, and occupational pressures are increasing. Patients attending tertiary care hospitals often experience multiple stressors, including financial difficulties, family responsibilities, work-related problems, and concerns regarding chronic disease management. However, limited research has explored the biological relationship between psychological stress markers and hypertension control among Pakistani patients. Most available studies have focused mainly on traditional risk factors, while the role of stress hormones remains insufficiently investigated.

A cross-sectional analytical study design provides an opportunity to evaluate the association between chronic stress indicators, cortisol levels, and blood pressure control among hypertensive patients. This design allows researchers to compare patients with controlled and uncontrolled hypertension and determine whether higher psychological stress scores and elevated cortisol levels are associated with poor blood pressure outcomes.

The present study will be conducted at a tertiary care hospital in Lahore, Pakistan, with the aim of investigating the relationship between chronic stress, cortisol levels, and uncontrolled hypertension. Understanding this association may provide valuable information for clinicians and public health professionals. It may encourage the integration of psychological assessment and stress

management strategies into routine hypertension care.

Early identification of stress-related factors may improve treatment outcomes because hypertension management should not only focus on medication but also address behavioral and psychological factors affecting cardiovascular health. Therefore, this study aims to provide evidence regarding the role of chronic stress and cortisol elevation as possible contributors to uncontrolled hypertension among patients in a tertiary healthcare setting.

MATERIALS AND METHODS

Study Design and Study Setting

This study was conducted using a **cross-sectional analytical study design** to assess the association between chronic psychological stress, cortisol levels, and uncontrolled hypertension among adult hypertensive patients. The study was carried out in the outpatient and hypertension clinics of a tertiary care hospital located in Lahore, Pakistan. A tertiary care hospital was selected because it receives patients from different socioeconomic backgrounds and provides specialized hypertension management services.

The study was conducted over a period of **six months** after approval from the institutional ethical review committee. The research followed the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before inclusion in the study.

Study Population

The study population consisted of adult patients diagnosed with hypertension and receiving follow-up care at the hospital. Patients were divided into two groups according to their blood pressure control status. Participants with blood pressure values within the recommended target range were categorized as the controlled hypertension group, whereas patients who failed to achieve target blood pressure levels despite treatment were classified as the uncontrolled hypertension group.

The purpose of selecting these two groups was to identify whether chronic stress levels and cortisol

concentrations differed between patients with controlled and uncontrolled blood pressure.

Sample Size and Sampling Technique

The sample size was calculated using the standard formula for cross-sectional analytical studies. The calculation was based on the expected prevalence of uncontrolled hypertension and previous findings regarding psychological stress and blood pressure association. After considering a confidence level of 95%, study power of 80%, and possible non-response, the required sample size was determined.

Participants were recruited through a **non-probability consecutive sampling technique**. All eligible patients visiting the hypertension clinic during the study period were approached and enrolled until the required sample size was achieved.

Inclusion Criteria

Participants were included according to the following criteria:

- Adults aged 18 years or above.
- Patients with a confirmed diagnosis of hypertension for at least six months.
- Patients currently taking antihypertensive medication or undergoing lifestyle management.
- Patients willing to participate and provide blood samples for cortisol assessment.
- Patients who provided written informed consent.

Exclusion Criteria

Participants were excluded if they had:

- Previously diagnosed endocrine disorders affecting cortisol production, such as Cushing syndrome or adrenal disease.
- Severe psychiatric illness requiring active psychiatric treatment.
- Current use of corticosteroid medications.
- Acute infection, severe inflammation, or critical illness during the study period.
- Pregnancy.

- Incomplete clinical or laboratory information.

Data Collection Procedure

Data collection was performed using a structured questionnaire developed after reviewing relevant literature. The questionnaire consisted of three major sections:

1. Demographic information

- Age
- Gender
- Residence
- Educational status
- Occupation
- Socioeconomic characteristics

2. Clinical characteristics

- Duration of hypertension
- Current antihypertensive medications
- Family history of hypertension
- Smoking status
- Physical activity level
- Body mass index (BMI)
- Presence of diabetes or other chronic diseases

3. Psychological stress assessment

Each participant was interviewed in a private environment to reduce discomfort and improve response accuracy.

Assessment of Chronic Stress

Chronic psychological stress was evaluated using a validated stress assessment questionnaire. The **Perceived Stress Scale (PSS-10)** was used to measure the participant's perception of stress during the previous month.

The scale contains ten questions related to feelings of unpredictability, lack of control, and emotional pressure. Each item was scored from 0 to 4, with higher scores indicating greater perceived stress. Participants were categorized into low, moderate, and high stress groups according to their total scores.

The use of a standardized psychological tool helped to measure stress levels in a systematic and reproducible manner.

Measurement of Cortisol Levels

Cortisol levels were assessed as a biological indicator of chronic stress. Blood samples were collected from participants under standardized conditions. Samples were collected during the morning hours because cortisol follows a daily rhythm, with higher concentrations generally observed in the early morning.

Approximately 5 ml of venous blood was collected using sterile techniques. Samples were transported to the hospital laboratory under appropriate conditions. Serum cortisol levels were measured using an enzyme-linked immunosorbent assay (ELISA) method according to the manufacturer's instructions.

Laboratory personnel performing cortisol analysis were blinded to the participant's hypertension control status to reduce measurement bias.

Blood Pressure Measurement

Blood pressure was measured according to standard clinical procedures. Participants were asked to sit quietly for at least five minutes before measurement. Blood pressure was recorded using a validated automated blood pressure device.

Two readings were taken at an interval of approximately one to two minutes, and the average value was considered for analysis. Proper cuff size was selected according to the participant's arm circumference to improve measurement accuracy.

Uncontrolled hypertension was defined according to clinical guidelines when blood pressure remained above the recommended target despite treatment.

Anthropometric Measurements

Body weight was measured using a calibrated weighing scale, while height was recorded using a standardized measuring scale. Body mass index was calculated using the formula:

$$\text{BMI} = \text{Weight (kg)} / \text{Height}^2 (\text{m}^2)$$

Participants were categorized according to standard BMI classifications.

Data Management and Statistical Analysis

Data were entered into statistical software for analysis. Continuous variables were presented as mean and standard deviation, while categorical variables were presented as frequencies and percentages.

The normality of continuous variables was assessed before statistical testing. The independent sample t-test or Mann-Whitney U test was applied for comparison between controlled and uncontrolled hypertension groups depending on data distribution.

The chi-square test was used to evaluate associations between categorical variables. Correlation analysis was performed to determine the relationship between stress scores, cortisol levels, and blood pressure measurements.

Multivariable logistic regression analysis was performed to identify independent predictors of uncontrolled hypertension after adjusting for possible confounding factors such as age, gender, BMI, duration of hypertension, and medication use.

A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of **240 hypertensive patients** were included in the analysis. Participants were divided into two groups according to their blood pressure control status. Among them, **120 patients had controlled hypertension**, while **120 patients were categorized as having uncontrolled hypertension**.

The mean age of the study participants was **54.6 ± 10.8 years**. The majority of participants were between 45 and 65 years of age. Male participants represented a slightly higher proportion of the study population compared with females. The two groups were comparable regarding age, gender distribution, duration of hypertension, and body mass index.

Patients with uncontrolled hypertension showed higher psychological stress scores and increased cortisol levels compared with patients who achieved adequate blood pressure control. The mean Perceived Stress Scale score was higher among uncontrolled hypertensive patients (**27.1 ±**

5.6) compared with controlled hypertensive patients (15.4 ± 4.8). Similarly, mean serum cortisol concentration was significantly elevated in the uncontrolled hypertension group (22.6 ± 6.3 $\mu\text{g/dL}$) compared with the controlled group (13.8 ± 4.5 $\mu\text{g/dL}$).

A positive relationship was observed between perceived stress levels, cortisol concentration, and systolic blood pressure. Patients with higher stress scores generally demonstrated increased systolic and diastolic blood pressure values.

Table 1. Demographic and Clinical Characteristics of Study Participants

Variables	Controlled (n=120)	Hypertension (n=120)	Uncontrolled (n=120)	Hypertension (n=120)	p-value
Age (years), Mean $\pm$ SD	53.8 $\pm$ 10.5		55.4 $\pm$ 11.1		0.28
Male gender, n (%)	67 (55.8%)		72 (60.0%)		0.51
Duration of hypertension (years)	6.2 $\pm$ 3.4		7.1 $\pm$ 3.8		0.06
BMI (kg/m ²)	27.4 $\pm$ 4.1		28.2 $\pm$ 4.5		0.15
Diabetes mellitus, n (%)	34 (28.3%)		46 (38.3%)		0.11
Current smokers, n (%)	18 (15.0%)		29 (24.2%)		0.08
Systolic BP (mmHg)	128.6 $\pm$ 7.8		154.9 $\pm$ 15.2		<0.001
Diastolic BP (mmHg)	78.4 $\pm$ 6.5		94.2 $\pm$ 10.1		<0.001

Table 2. Association of Stress Scores and Cortisol Levels with Hypertension Control Status

Parameters	Controlled (n=120)	Hypertension (n=120)	Uncontrolled (n=120)	Hypertension (n=120)	p-value
Perceived Stress Score	15.4 $\pm$ 4.8		27.1 $\pm$ 5.6		<0.001
Serum cortisol ($\mu\text{g/dL}$)	13.8 $\pm$ 4.5		22.6 $\pm$ 6.3		<0.001
Low stress category, n (%)	62 (51.7%)		18 (15.0%)		<0.001
Moderate stress category, n (%)	45 (37.5%)		54 (45.0%)		
High stress category, n (%)	13 (10.8%)		48 (40.0%)		
Cortisol above reference range, n (%)	21 (17.5%)		71 (59.2%)		<0.001

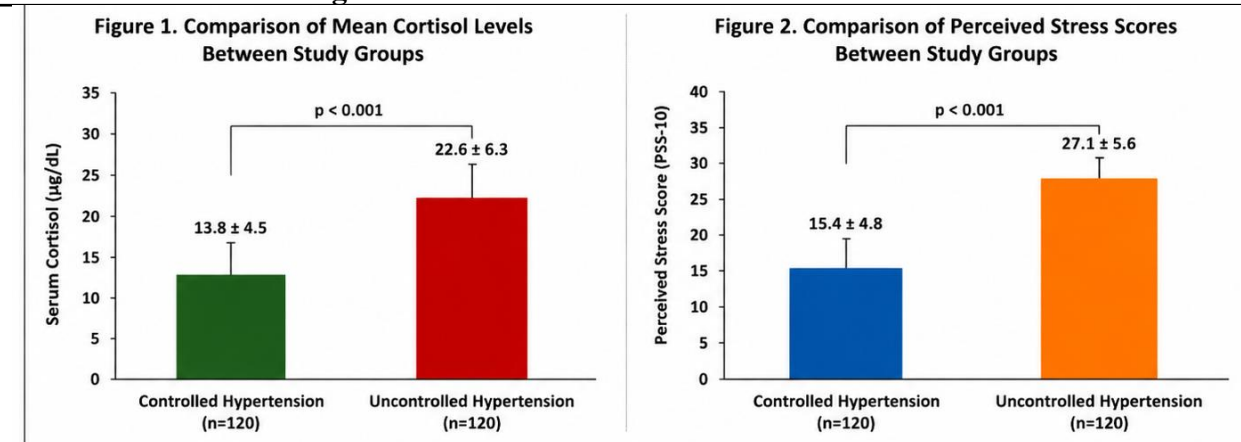


Figure 1: Comparison of mean cortisol levels between controlled and uncontrolled hypertension groups.

Figure 2: Comparison of perceived stress scores between controlled and uncontrolled hypertension groups.

The graphical analysis demonstrated a clear increase in both stress scores and cortisol concentration among patients with uncontrolled blood pressure.

DISCUSSION

The present study evaluated the relationship between chronic psychological stress, cortisol levels, and uncontrolled hypertension among hypertensive patients attending a tertiary care hospital in Lahore, Pakistan. The findings showed that patients with uncontrolled hypertension had significantly higher perceived stress scores and increased serum cortisol levels compared with patients who achieved blood pressure control. These results suggest that psychological stress and biological stress responses may contribute to poor hypertension control and should be considered important factors during routine hypertension management.

In this study, patients with uncontrolled hypertension demonstrated markedly higher stress scores compared with controlled hypertensive patients. This finding supports previous evidence showing that chronic psychosocial stress is associated with adverse cardiovascular outcomes. Steptoe and Kivimäki (2013) reported that long-term exposure to psychological stress activates physiological pathways that increase cardiovascular risk, including hypertension development and progression. Chronic stress may influence cardiovascular function through

repeated activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, resulting in increased vascular tone, inflammation, and metabolic disturbances.

The increased cortisol concentration observed among uncontrolled hypertensive patients represents an important biological finding of this study. Cortisol is a major hormone involved in stress adaptation; however, continuous elevation due to prolonged stress exposure may become harmful. Persistent cortisol elevation can increase blood pressure through several mechanisms, including enhanced sensitivity to catecholamines, sodium retention, impaired endothelial function, and increased vascular resistance. McEwen described this phenomenon as a consequence of chronic stress-related allostatic load, where repeated activation of stress systems produces physiological damage rather than protection (McEwen, 2006).

The present findings are consistent with previous studies suggesting that cortisol may serve as a useful biomarker of chronic stress-related cardiovascular risk. Iob and Steptoe (2019) highlighted that hair cortisol concentration provides an indicator of long-term cortisol exposure and has potential value in cardiovascular

research because it reflects prolonged stress activity rather than temporary hormonal changes. Although the current study measured serum cortisol, the observed association between higher cortisol levels and uncontrolled blood pressure supports the possible role of stress biomarkers in identifying patients at increased risk of poor hypertension outcomes.

A possible explanation for the relationship between stress and uncontrolled hypertension is the continuous stimulation of the sympathetic nervous system. Chronic psychological stress increases sympathetic activity, causing increased heart rate, cardiac output, and peripheral vascular resistance. Over time, these repeated responses may contribute to sustained elevation of blood pressure. Previous research has demonstrated that individuals experiencing chronic stress have greater cardiovascular reactivity and may develop impaired blood pressure regulation (Dimsdale, 2008). Similar mechanisms may explain why some patients in the present study remained hypertensive despite receiving antihypertensive treatment.

Another important observation was the higher proportion of patients with high stress levels in the uncontrolled hypertension group. This finding suggests that psychological factors may influence treatment outcomes beyond traditional risk factors. Patients experiencing continuous emotional pressure may have difficulty maintaining healthy behaviors, including regular medication use, physical activity, dietary control, and adequate sleep. Stress-related behavioral changes can indirectly worsen hypertension control. Cohen et al. (2007) emphasized that psychological stress affects disease risk through both biological pathways and changes in health-related behaviors.

The results are particularly important in the context of Pakistan, where patients attending tertiary care hospitals frequently experience multiple social and economic stressors. Financial concerns, occupational pressure, family responsibilities, and limited healthcare resources may increase psychological stress among patients with chronic diseases. Despite the high burden of

hypertension in Pakistan, routine clinical care often focuses mainly on medication adjustment and lifestyle counseling, while psychological assessment is rarely included. The findings of this study highlight the need for a more comprehensive approach that considers emotional and biological stress factors during hypertension management.

The observed association between cortisol and blood pressure control does not necessarily indicate direct causation because of the cross-sectional design of this study. Since measurements were taken at a single point in time, it is not possible to determine whether increased cortisol caused poor blood pressure control or whether uncontrolled hypertension increased psychological stress. However, the significant relationship between stress scores, cortisol levels, and blood pressure suggests an important interaction that requires further investigation through longitudinal studies.

The findings also have clinical implications. Screening hypertensive patients for psychological stress may help identify individuals who are at greater risk of uncontrolled blood pressure. Incorporating stress management strategies, such as relaxation techniques, behavioral therapy, improved sleep management, and patient counseling, may provide additional benefits alongside pharmacological treatment. Previous cardiovascular research has emphasized that stress reduction should be considered as part of a multidimensional approach for patients with cardiovascular risk factors (Steptoe & Kivimäki, 2013).

This study has several strengths. It evaluated both psychological and biological indicators of stress rather than relying only on self-reported stress levels. The use of cortisol measurement provided objective evidence supporting the relationship between chronic stress and hypertension control. Additionally, studying patients from a tertiary care hospital in Lahore provides valuable local information regarding stress-related factors among Pakistani hypertensive patients.

However, some limitations should be acknowledged. The cross-sectional design limits

the ability to establish cause-and-effect relationships. Cortisol levels may also be influenced by factors such as sleep pattern, medication use, acute illness, and timing of sample collection. Furthermore, psychological stress was assessed through self-reported responses, which may be influenced by individual perception. Future prospective studies with larger populations and repeated cortisol measurements are recommended to better understand the long-term relationship between stress and hypertension.

In conclusion, this study demonstrates that uncontrolled hypertension is associated with higher psychological stress levels and increased cortisol concentrations. These findings support the concept that chronic stress-related biological changes may contribute to difficulty achieving blood pressure control. Integrating stress assessment and management into hypertension care may improve treatment outcomes and provide a more holistic approach for patients with cardiovascular disease.

CONCLUSION

This study highlights an important relationship between chronic psychological stress, cortisol levels, and poor blood pressure control among hypertensive patients. The findings suggest that individuals with uncontrolled hypertension experience greater psychological stress and demonstrate higher cortisol concentrations compared with patients who maintain adequate blood pressure control. These observations support the concept that stress-related physiological changes may contribute to difficulties in achieving optimal hypertension management. Chronic stress has been recognized as an important factor that can influence cardiovascular health through repeated activation of stress pathways, including the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis.

The increased cortisol levels observed among patients with uncontrolled hypertension indicate that prolonged activation of stress mechanisms may have a role in blood pressure regulation. Persistent cortisol elevation can affect vascular

function, increase cardiovascular strain, and promote conditions that favor sustained hypertension. Previous research has also suggested that increased cortisol exposure may be associated with higher hypertension risk, supporting the biological findings observed in this study.

The results emphasize that hypertension management should not focus only on pharmacological treatment and traditional risk factors. Psychological stress assessment may provide additional information for identifying patients who are more likely to have uncontrolled blood pressure. Incorporating stress reduction approaches, patient counseling, and behavioral interventions along with standard antihypertensive therapy may improve overall treatment outcomes.

In the Pakistani healthcare setting, where patients often experience social, economic, and disease-related stress, addressing psychological factors may be particularly valuable. Routine evaluation of stress levels and consideration of biological stress markers such as cortisol could support a more complete approach to hypertension care.

Although the cross-sectional design limits the ability to establish a direct cause-and-effect relationship, the findings provide evidence of a significant association between chronic stress, elevated cortisol levels, and uncontrolled hypertension. Future longitudinal studies involving larger populations and repeated hormonal measurements are recommended to further clarify the direction of this relationship.

In conclusion, chronic stress appears to be an important contributor associated with poor hypertension control. Recognizing stress as part of cardiovascular risk assessment may help clinicians develop more effective, patient-centered strategies for controlling hypertension and reducing future cardiovascular complications.

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