# Association between physical activity and resistant hypertension in treated hypertension patients: analysis of the national health and nutrition examination survey 

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#### Abstract

Introduction Current guidelines suggest that regular aerobic training might lower blood pressure in hypertensive individuals. However, evidence linking resistant hypertension (RH) with total daily physical activity (PA), including work-, transport-, and recreation-related PA, is limited. Therefore, this study assessed the association between daily PA and RH.

Method A cross-sectional study was conducted using data acquired from a nationwide survey in the US (the National Health and Nutrition Examination Survey, NHANES). The weighted prevalence of RH was calculated, and moderate and vigorous daily PA was assessed using the Global Physical Activity Questionnaire (GPAQ). A multivariate logistic regression model determined the association between daily PA and RH. Results A total of 8,496 treated hypertension patients were identified, including 959 RH cases. The unweighted prevalence of RH among treated hypertension cases was $11.28 \%$, while the weighted prevalence was $9.81 \%$. Participants with RH had a low rate of recommended PA levels (39.83\%), and daily PA and RH were significantly associated. PA exhibited significant dose-dependent trends with a low probability of RH (p-trends < 0.05 ). Additionally, participants with sufficient daily PA had a $14 \%$ lower probability of RH than those with insufficient PA [fully adjusted odds ratio $(O R)=0.86 ; 95 \%$ confidence interval $(C l)=0.74-0.99)$. Conclusion The present study revealed that RH has an incidence of up to $9.81 \%$ in treated hypertension patients. Hypertensive patients tended to be physically inactive, and insufficient PA and RH were significantly associated. Sufficient daily PA should be recommended to reduce the RH probability among treated hypertension patients. Keywords Physical activity, Resistant hypertension, National Health and Nutrition Examination Survey, Global physical activity questionnaire, Prevalence, Risk


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## Introduction

Uncontrolled hypertension is a critical cardiovascular risk factor that increases the risk of coronary artery disease, heart failure, stroke, and chronic kidney disease progression [1]. However, many hypertensive patients develop resistant hypertension (RH) after treatment. RH is defined as a condition in which the blood pressure remains above the recommended levels despite administering optimum doses of three or more classes of antihypertensive drugs, including a diuretic, or if target blood pressure control requires four or more classes of antihypertensive drugs [2-6]. Previous studies have revealed that RH is strongly associated with a high risk of cardiovascular events and all-cause mortality [1, 7].
Besides medication, current guidelines recommend lifestyle modification for blood pressure control in RH patients, including weight reduction, consuming a diet rich in fruits and vegetables, low-fat dairy products, a low-salt diet, smoking cessation, and regular aerobic physical activity (PA) [4, 6, 8]. Regular PA can reduce the blood pressure of individuals with hypertension [9]. A Consensus Document from the European Association of Preventive Cardiology (EAPC) and the ESC Council on Hypertension recommends regular aerobic training in hypertensive patients, while dynamic resistance training is recommended in high-normal hypertension patients [10]. However, evidence on PA implementation for blood pressure management has been relatively limited in prescribed exercise [9]. Additionally, the association between RH and the total amount of daily PA, including work-, transport-, and recreation-related PA, remains unclear. Therefore, we determined the association between daily PA and RH using data from a nationwide US survey (the National Health and Nutrition Examination Survey, NHANES). We hypothesized that sufficient daily PA could reduce the RH probability in treated hypertension patients.

## Methods

## Study Population

First, we retrieved data from the National Health and Nutrition Examination Survey (NHANES) conducted by the National Center for Health Statistics. The NHANES uses data collected from a cross-sectional sample of the noninstitutionalized US civilian population to evaluate its health and nutritional status [11]. About 12,000 people are required to participate in the NHANES every two-year cycle. The percentage agreeing to participate varies from year to year. Of the initial 12,000, an average of 10,500 agreed to complete home interviews, and about 10,000 finished the data collection in the Mobile Test Center [12]. All procedures of the NHANES were approved by the National Center for Health Statistics
institutional review board and written informed consent was obtained from all participants.
We examined data from seven consecutive NHANES cycles (2005-2018). We included nonpregnant participants $>20$ years old, comprising 45,000 participants. Then, we excluded those with missing blood pressure and PA questionnaire data. Next, we excluded participants under 20 years, pregnant, had no history of hypertension, had not used antihypertensive medication, and had not received adequate antihypertensive therapy (defined as blood pressure $\geq 140 / 90 \mathrm{mmHg}$ but received less than three antihypertensive medications, or had not used diuretics) (Fig. 1). The final study population consisted of 5000 participants.

## Definition of terms

The NHANES complied with current guidelines for blood pressure measurement [13, 14]. Three consecutive blood pressure measurements were taken to obtain an accurate measurement, and the average values of three consecutive systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements were calculated. The nurses who took blood pressure measurements obtained certification through a Shared Care Research and Education Consulting training program. Resistant hypertension (RH) was defined as a condition in which the blood pressure remains above the recommended levels despite the administration of optimum doses of three or more classes of antihypertensive drugs, including a diuretic, or if target blood pressure control requires four or more classes of antihypertensive drugs [2-6]. Uncontrolled blood pressure was defined as an average SBP $>140 \mathrm{mmHg}$ or DBP $>90 \mathrm{mmHg}$ while on treatment. Antihypertensive medication use was self-reported.

## Assessment of physical activity

Participants were asked to complete the Global Physical Activity Questionnaire (GPAQ) to assess PA [15, 16]. The GPAQ was developed by the World Health Organization (WHO) in 2002 in response to a greater interest in the role of PA in health $[15,16]$. It collects information based on three domains (work, travel to and from places, and recreational activities) and sedentary behavior.

The WHO recommends that adults perform moderateintensity PA for at least 150 min , vigorous-intensity PA for 75 min , or an equivalent combination of moderateand vigorous-intensity PA achieving at least 600 metabolic equivalents (MET) minutes every week (Table 1) [16]. Similarly, according to the Physical Activity Guidelines for Americans, adults must engage in moderateintensity PA for at least 150-300 min, vigorous-intensity aerobic PA for 75-150 min, or an equivalent combination of moderate- and vigorous-intensity aerobic PA every week (Table 1) [17]. In the present study, if the exercise


Fig. 1 Flowchart illustrating the recruitment criteria of the study population
intensity and time met the above requirements, it was considered PA sufficient. Otherwise, it was defined as PA insufficient. Additionally, the MET-minutes per week was calculated to estimate PA and obtain continuous variables for the dose-dependent analysis. Moreover, American guidelines suggest that doing PA beyond the equivalent of 300 min of moderate-intensity PA can provide additional health benefits. Therefore, participants who surpassed this were described as having overfulfilled PA (PA overfulfilled). A detailed description is presented in Table 1.

## Covariates

We included demographic variables, smoking status (either ever smoked or have never smoked), body mass index (BMI, $\mathrm{kg} / \mathrm{m}^{2}$ ), total cholesterol ( $\mathrm{mg} / \mathrm{dL}$ ), aspartate aminotransferase (AST, IU/L), alanine aminotransferase (ALT, IU/L), estimated glomerular filtration rate (eGFR, estimated using the Modification of Diet in Renal

Disease 4-variable Eq. 1 [18]), total nutrient intake per day [sodium (mg), energy (kcal), and fat (gm)] as covariates. Demographic variables included sex, age, race (nonHispanic blacks or other races), family poverty index ratio (PIR), and marital status (married, unmarried, or another status).

## Statistical analysis

Continuous variables are expressed as means $\pm$ standard deviations or medians (interquartile ranges, IQR), whereas categorical variables are presented as cases ( n ) and percentages (\%). Non-normal distributions were transformed by conducting natural log or Box-Cox transformations. For comparisons between continuous variables, normally distributed data were analyzed using Student's $t$-test, whereas non-normally distributed data were analyzed using Wilcoxon signed-rank test. Categorical variables were analyzed using $\chi$ [2] tests. To ensure a national representation, the weighted RH prevalence

Table 1 Recommended physical activity levels per week

|  |  | Recommendation $A^{a}$ | Recommendation $B^{a}$ | Recommendation $\mathrm{C}^{\text {a }}$ | Recom-mendation D ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Recommendations by WHO [16] | Time spent | At least 150 min of moderate-intensity PA | At least 75 min of vigorous-intensity PA |  |  |
|  | MET values <br> b | ```At least 150 min * 4.0 =600 MET-minutes }\mp@subsup{}{}{\mathrm{ c}``` | $\begin{aligned} & \text { At least } \\ & 75 \text { min * } 8.0 \\ & =600 \\ & \text { MET-minutes }{ }^{\text {d }} \end{aligned}$ | Equivalent combination of moderate- and vigorousintensity PA $>600$ MET-minutes ${ }^{\text {e }}$ |  |
| Guideline for Americans [17] | Time spent | 150 to 300 min of moderate-intensity PA | 75 to 150 min of vigorous-intensity PA | Equivalent combination of moderate- and vigorousintensity PA | Beyond the equivalent of 300 min of moderateintensity PA |

PA, physical activity; METs, metabolic equivalents; WHO, World Health Organization
${ }^{\text {a }}$ Based on the recommendations of the WHO and the American guidelines, participants who meet either Recommendation A, Recommendation B, or Recommendation C are described as having achieved sufficient physical activity ( $\mathrm{PA}_{\text {sufficient }}$ ). Participants who meet Recommendations D are described as having overfulfilled physical activity ( $\mathrm{PA}_{\text {overfulfilled }}$ ).
${ }^{\mathrm{b}}$ MET values are applied to the time variables to assess the intensity (moderate or vigorous) of PA.
${ }^{\text {c }}$ MET values of moderate-intensity work, moderate-intensity recreation, and transport (cycling and walking) are equivalent to 4.0
${ }^{d}$ MET values of vigorous-intensity work and vigorous-intensity recreation are equivalent to 8.0
${ }^{e}$ An equivalent combination of MET values of moderate- and vigorous-intensity physical activity
was calculated in line with the analytical guidelines of the National Center for Health Statistics. An unweighted logistic regression model was also applied to analyze the association between PA and RH since cases with special health concerns were excluded. The effect estimates were reported as odds ratios (ORs) and $95 \%$ confidence intervals (CIs). Statistical analyses were performed using IBM SPSS Statistics (v. 24.0, IBM Corp., Armonk, NY, USA) and R (v. 3.6.0). A $p<0.05$ was considered statistically significant.

## Results

## Characteristics of the participants

First, we retrieved data on 59,843 participants from seven consecutive National Health and Nutrition Examination Survey (NHANES) cycles (2005-2018). Among them, 8,496 cases of treated hypertension were screened, including 959 cases of resistant hypertension (RH). The unweighted prevalence of RH among treated hypertension cases was $11.28 \%$, and the weighted prevalence was 9.81\%.

After the screening, 6,049 participants were finally enrolled (Fig. 1), including 2852 men and 3197 women aged 20 to 80 years (median age, 63 years). RH participants were older, with a higher proportion of men ( $50.78 \%$ vs. $46.46 \%$ ) than non-RH. Most participants with hypertension did not meet the recommended daily PA levels (only $46.60 \%$ attained the recommended PA levels). The two groups significantly differed for race, family PIR, marital status, BMI, total cholesterol, eGFR, nutrient
intake, and ALT ( $\mathrm{p}<0.05$ ). Detailed descriptions of participant characteristics are presented in Table 2.

The results of the multivariate regression analyses are summarized in Table 3. In the unadjusted model, the PA index (MET-minutes per week, Box-Cox transformed) was negatively correlated with $\mathrm{RH}(\mathrm{OR}=0.95$, $95 \%$ CI: $0.93-0.96, \mathrm{p}<0.05$ ). After adjusting for confounding factors, the negative correlation between PA and RH remained significant in model $2(\mathrm{OR}=0.96$, 95\% CI: 0.94-0.98, $\mathrm{p}<0.001$ ) and model 3 ( $\mathrm{OR}=0.97$, $95 \%$ CI: $0.95-0.99, \mathrm{p}<0.001$ ). Daily PA exhibited significant dose-dependent trends with a low RH probability (p-trends $<0.05$ ) when PA was set as the categorical variable (quartiles).

According to the recommendations of the WHO and Physical Activity Guidelines for Americans, patients were classified as $\mathrm{PA}_{\text {sufficient }}$ and $\mathrm{PA}_{\text {insufficient }}$ (Table 1). The univariate analysis showed that $\mathrm{PA}_{\text {sufficient }}$ was significantly associated with RH ( $O R=0.72$; $95 \% C I=0.63-0.83$ ). After adjusting for demographic variables (model 2), $\mathrm{PA}_{\text {sufficient }}$ was still significantly associated with $\mathrm{RH}(O R=0.79 ; 95 \%$ $C I=0.68-0.92$ ). In model 3, participants with sufficient PA had a $14 \%$ lower probability of RH than those with insufficient PA after adjusting for confounding factors ( $O R=0.86$; 95\% $C I=0.74-0.99$ ) (Table 4).
Moreover, $\mathrm{PA}_{\text {overfulfilled }}$ was used as a variable for regression analysis based on the Physical Activity Guidelines for Americans. The associations between $\mathrm{PA}_{\text {overfulfilled }}$ and RH in multivariate sequential models are presented in Table 5. $\mathrm{PA}_{\text {overfulfilled }}$ participants had a significantly lower probability of RH. The fully adjusted $O R$ between

Table 2 Baseline characteristics of the study population

| Characteristics | All patients | Resistant hypertension group $N=959$ | Non-resistant hypertension group $N=5,090$ | $P$ value |
| :---: | :---: | :---: | :---: | :---: |
| Age |  |  |  | <0.001 |
| 20-35 years | 128 (2.1\%) | 9 (0.94\%) | 119 (2.34\%) |  |
| 36-50 years | 869 (14.4\%) | 80 (8.34\%) | 789 (15.50\%) |  |
| 51-65 years | 2301 (38.0\%) | 299 (31.18\%) | 2002 (39.33\%) |  |
| Over 65 years | 2751 (45.5\%) | 571 (59.54\%) | 2180 (42.83\%) |  |
| Sex |  |  |  | $<0.05$ |
| Male | 2852 (47.1\%) | 487 (50.78\%) | 2365 (46.46\%) |  |
| Female | 3197 (52.9\%) | 472 (49.22\%) | 2725 (53.54\%) |  |
| Race ${ }^{1}$ |  |  |  | $<0.001$ |
| Non-Hispanic Blacks | 1676 (27.7\%) | 379 (39.52\%) | 1297 (25.48\%) |  |
| Other races | 4373 (72.3\%) | 580 (60.48\%) | 3793 (74.52\%) |  |
| Family PIR ${ }^{2}$ |  |  |  | $<0.01$ |
| $\leq 1.85$ | 2406 (39.8\%) | 407 (42.44\%) | 1999 (39.27\%) |  |
| > 1.85 | 3082 (51.0\%) | 446 (46.51\%) | 2636 (51.79\%) |  |
| Unknown | 561 (9.3\%) | 106 (11.05\%) | 455 (8.94\%) |  |
| Marital status |  |  |  | <0.05 |
| Married | 3318 (54.9\%) | 486 (50.68\%) | 2832 (55.64\%) |  |
| Unmarried | 2214 (36.6\%) | 385 (40.15\%) | 1829 (35.93\%) |  |
| Other status | 517 (8.5\%) | 88 (9.18\%) | 429 (8.43\%) |  |
| Former and current smoker | 3030 (50.09\%) | 519 (54.12\%) | 2511 (49.33\%) | $<0.01$ |
| Body mass index ${ }^{3}$ |  |  |  | <0.01 |
| $<25 \mathrm{~kg} / \mathrm{m}^{2}$ | 873 (14.4\%) | 118 (12.3\%) | 755 (14.8\%) |  |
| $25-30 \mathrm{~kg} / \mathrm{m}^{2}$ | 1864 (30.8\%) | 261 (27.2\%) | 1603 (31.5\%) |  |
| $>30 \mathrm{~kg} / \mathrm{m}^{2}$ | 3312 (54.8\%) | 580 (60.5\%) | 2732 (53.7\%) |  |
| Log (ALT) ${ }^{4}$ | $3.08 \pm 0.44$ | $3.04 \pm 0.44$ | $3.09 \pm 0.44$ | $<0.001$ |
| Log (AST) ${ }^{5}$ | $3.18 \pm 0.34$ | $3.16 \pm 0.33$ | $3.18 \pm 0.34$ | $>0.05$ |
| Total cholesterol (mg/dL) | $4.79 \pm 1.06$ | $4.67 \pm 1.11$ | $4.82 \pm 1.05$ | $<0.001$ |
| eGFR <br> ( $\mathrm{mL} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ ) | $76.37 \pm 23.86$ | $68.18 \pm 24.89$ | $77.92 \pm 23.34$ | <0.001 |
| Sodium intake (mg/d) | $3189.55 \pm 1588.37$ | $3066.58 \pm 1495.92$ | $3212.72 \pm 1604.28$ | <0.05 |
| Energy intake (kcal/d) | $1893.29 \pm 828.03$ | $1807.65 \pm 783.65$ | $1909.43 \pm 835.22$ | $<0.001$ |
| Fat intake (gm/d) | $74.24 \pm 40.95$ | $70.61 \pm 40.09$ | $74.92 \pm 41.08$ | <0.05 |
| Metabolic Equivalents (METs) | $\begin{gathered} 480.00 \\ (0.00-2160.00) \end{gathered}$ | $\begin{gathered} 216.00 \\ (0.00-1440.00) \end{gathered}$ | $\begin{gathered} 480.00 \\ (0.00-2400.00) \end{gathered}$ | <0.001 |
| With sufficient PA | 2819 (46.60\%) | 382 (39.83\%) | 2437 (47.88\%) | <0.001 |

eGFR, estimated glomerular filtration rate; PA, physical activity; PIR, poverty index ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase;
${ }^{1}$ Considering the impact of race on resistant hypertension, race was divided into non-Hispanic blacks and other races (Mexican Americans, other Hispanics, nonHispanic whites, non-Hispanic Asians, and others);
${ }^{2}$ Below poverty level was defined as PIR $<1.85$, above poverty level was defined as PIR $>1.85$;
${ }^{3}$ Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Overweight was defined as $\mathrm{BMI} \geq 25 \mathrm{~kg} / \mathrm{m}^{2} \mathrm{and}$ $<30 \mathrm{~kg} / \mathrm{m}^{2}$, and obesity was defined as BMI $\geq 30 \mathrm{~kg} / \mathrm{m}^{2}$;
${ }^{4} \log$ (ALT), natural logarithm of ALT;
${ }^{5} \mathrm{Log}$ (AST), natural logarithm of AST;
overfulfilled and insufficient PA groups was 0.83 (95\% $C I=0.70-0.98$ ).

## Discussion

In the current study, the prevalence of resistant hypertension (RH) was up to $9.81 \%$, slightly lower than previous studies, ranging from 12 to $14 \%{ }^{2}$. This variation could be attributed to the relatively strict screening criteria,
excluding treated hypertension patients who received inadequate treatment or had no recommended treatment strategy.

Patients with RH have poor cardiovascular outcomes. Therefore, it is necessary to use a comprehensive treatment strategy to enhance blood pressure control in these patients [1]. Previous studies have presented biological evidence to support the role of PA in lowering blood

Table 3 Association between physical activity and resistant hypertension

|  | Odds ratios (95\% confi- |  |  |
| :--- | :--- | :--- | :--- |
| dence interval) |  |  |  |

${ }^{a}$ Model 1 was unadjusted
${ }^{\text {b }}$ Model 2 was adjusted for age, sex, race, family poverty index ratio (PIR), and marital status
${ }^{\text {c }}$ Model 3 was adjusted for variables in Model $2+$ smoking status, BMI, total cholesterol, aspartate aminotransferase (natural log transformed), alanine aminotransferase (natural log transformed), estimated glomerular filtration rate, dietary sodium, dietary energy, and dietary fat
${ }^{\text {d }}$ Data were Box-Cox transformed. MET-minutes per week were used to assess the intensity (moderate or vigorous) of physical activity
pressure. Multiple mechanisms are involved in the adaptation of blood pressure to PA [19]. Sufficient PA can
reduce systemic vascular resistance via decreased activities of the sympathetic nervous and the renin-angiotensin systems [20]. Moreover, PA can improve endotheliumdependent vasodilatation and enhance baroreceptor sensitivity and arterial compliance [20].

Guidelines recommend lifestyle interventions for managing hypertension [10, 21]. Randomized controlled trials have demonstrated the effects of aerobic PA in blood pressure control [9]. However, evidence for the implementation of PA in blood pressure management has been relatively limited in prescribed exercise. In most previous studies, aerobic activity was defined in detail regarding intensity, frequency and duration. Further, the medical ergometer cycle is the most frequently used way to implement aerobic activities. Notably, many individuals spontaneously participate in daily PA but not in a prescribed scheme [15, 22]. Nevertheless, few studies have investigated the effects of daily PA on hypertension, especially RH. It is unclear whether daily PA, not prescribed exercise, can also contribute to controlling blood pressure. Hence, we determined the relationship between daily PA and RH probability in treated hypertension patients.
Hypertensive patients tended to be physically inactive (46.6\%). RH participants had lower rates of meeting the recommended PA levels than those without RH (39.83 and $47.88 \%$, respectively). Previous studies have found that physical inactivity might account for 5-13\% of hypertension risk [9]. The current study also observed strong associations between daily PA and RH probability in treated hypertension patients. After adjusting for demographic factors, dietary factors, and laboratory results, sufficient daily PA revealed an important role in

Table 4 Association between sufficient physical activity and resistant hypertension

|  | Model A [1] |  | Model B [2] |  | Model C [3] |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | OR P |  | OR P |  | OR P |  |
| Insufficient physical activity | Reference |  | Reference |  | Reference |  |
| Sufficient physical activity | 0.72 (0.63,0.83) | $<0.01$ | 0.79 (0.68,0.92) | $<0.05$ | 0.86(0.74,0.99) | $<0.05$ |

RH, resistant hypertension; OR, odds ratio
${ }^{[11]]}$ Model A was unadjusted
${ }^{[[2]]}$ Model B was adjusted for age, sex, race, family poverty index ratio (PIR), and marital status
${ }^{[[3]]}$ Model C was adjusted for variables in Model $2+$ smoking status, BMI, total cholesterol, aspartate aminotransferase, alanine aminotransferase, estimated glomerular filtration rate, dietary sodium, dietary energy, and dietary fat

Table 5 Association between overfulfilled physical activity and resistant hypertension

|  | Model $1^{\text {a }}$ |  | Model $\mathbf{2}^{\text {b }}$ |  | Model $3^{\text {c }}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | OR P |  | OR P |  | OR P |  |
| Comparison with insufficient PA group |  |  |  |  |  |  |
| Overfulfilled physical activity group | 0.69 (0.59,0.81) | <0.01 | $\begin{aligned} & 0.77(0.65, \\ & 0.90) \end{aligned}$ | $<0.01$ | 0.83(0.70, 0.98) | $<0.05$ |
| OR, odds ratio |  |  |  |  |  |  |
| ${ }^{\text {a }}$ Model 1 was unadjusted |  |  |  |  |  |  |
| ${ }^{\text {b }}$ Model 2 was adjusted for age, sex, race, family poverty index ratio (PIR), and marital status |  |  |  |  |  |  |
| ${ }^{\text {c }}$ Model 3 was adjusted for variables in Model $2+$ smoking status, BMI, total cholesterol, aspartate aminotransferase (natural log transformed), alanine aminotransferase (natural log transformed), estimated glomerular filtration rate, dietary sodium, dietary energy, and dietary fat |  |  |  |  |  |  |

lowering RH probability, with clinically relevant treatment effects. Moderate-intensity daily PA for at least 150 min , vigorous-intensity daily PA for at least 75 min , or an equivalent combination of moderate- and vigorousintensity daily PA effectively reduced RH probability in treated hypertension patients.
Based on our results, the daily PA mentioned above can be recommended to reduce RH probability in treated hypertension patients. Daily PA is as effective as prescribed exercise to reduce RH probability. The present study defines daily PA in three settings: work, travel to and from places, and recreational activities. Specifically, the following moderate-intensity daily PA can be recommended to reduce RH risk [16]: (1) daily work leading to small increases in breathing or heart rate (e.g., brisk walking or carrying light loads), (2) walking or bicycle for commuting, (3) sports, fitness or recreational activities leading to a mildly accelerated breathing or heart rate (e.g., brisk walking, cycling, swimming, volleyball). Moreover, the following vigorous-intensity daily PA can also be recommended [16]: (1) daily work leading to large increases in breathing or heart rate (e.g., carrying heavy loads, digging, or construction work), (2) sports, fitness, or recreational activities leading to significantly accelerated breathing or heart rates (e.g., running or football).

To determine whether there was an additional benefit from further increases in PA, we introduced another variable, the overfulfilled PA, defined as PA beyond 300 min of moderate-intensity PA. Overfulfilled PA could reduce the RH probability by $17 \%$ compared to insufficient PA. As mentioned above, moderate-intensity daily PA for at least 150 min or vigorous-intensity daily PA for at least 75 min comprises sufficient PA, reducing the RH probability by $14 \%$ compared to insufficient PA. Thus, the advantage of 300 min of moderate-intensity PA (overfulfilled PA) was less pronounced compared to sufficient PA. The effectiveness of the daily PA is probably dose-dependent and increases with increasing dosage. After fully adjusting for confounding factors, daily PA exhibited significant dose-dependent trends with a low RH probability when PA was the categorical variable (quartiles). Based on our results, adverse blood pressure response was not observed in overfulfilled exercising. Consequently, taking as much daily PA as possible could have further increased the reduction in RH probability. However, the additional benefit of overfulfilled PA compared to sufficient PA was small, and adherence to overfulfilled PA is a challenge to most patients. It is more reasonable to recommend basic sufficient PA for most hypertensive patients to reduce the RH probability [23].

## Strengths and limitations

The major strengths of the present study included using a large sample size, which increased the power of our
findings. The prevalence of RH among treated hypertension cases was reliable since a nationally representative sample of the US population was used. Additionally, the detailed information collected from the NHANES included a wide range of potential confounders, such as dietary intakes and laboratory results. Moreover, since 1999, the NHANES survey has become a continuous program focusing on various health and nutrition measurements. As a continuous program, it has a mature and reliable sampling process and methodological procedures across the surveys. To the best of our knowledge, the present study is the first to investigate the association between daily PA and RH probability based on a nationwide database. Second, The GPAQ is a valid and reliable tool for measuring PA. Although wearable devices improve the objectivity and accuracy of PA measurement, self-reported survey methods still confer the advantage of covering the general population due to their low cost [15]. Assessment by GPAQ can distinguish the true effect of the daily PA, closer to a real-life spontaneous PA situation, which has led to reliable results for the relationship between daily PA and RH.

However, the present study also has some limitations. First, the cross-sectional design made causal inference problematic. Therefore, further studies involving highquality prospective cohorts should be conducted to validate the present findings. Second, the blood pressure measurements included only office blood pressure but not ambulatory blood pressure measurements. Third, we did not consider the optimal dosage of each medication. However, medication use and dosage represented realworld management preferences, which effectively reflect PA effects in patients treated for hypertension.

## Conclusion

In summary, we showed that RH has an incidence of up to $9.81 \%$ in treated hypertension patients. Hypertensive patients tended to be physically inactive, and most of them, especially RH, did not perform sufficient PA. Furthermore, we found a significant association between insufficient daily PA and RH probability. Thus, sufficient PA should be recommended to reduce RH probability. Although this beneficial effect was dose-dependent and overfulfilled PA presented additional protection against RH, those who achieved sufficient PA (based on the PA guidelines) were also less prone to RH than those insufficiently active.

| Abbreviations |  |
| :--- | :--- |
| ALT | alanine aminotransferase |
| AST | aspartate aminotransferase |
| eGFR | estimated glomerular filtration rate |
| GPAQ | Global Physical Activity Questionnaire |
| NHANES | National Health and Nutrition Examination Survey |
| PA | physical activity |
| PIR | Poverty index ratio |


| RH | resistant hypertension |
| :--- | :--- |
| WHO | World Health Organization |

## Acknowledgements

This study analyzed data provided by the National Health and Nutrition Examination Survey (NHANES).

## Authors' contributions

Weidai Zhang, Chumin Ni and Ronghe Xu created the study conception and design. Zhixiong Cai, Chumin Ni, Xiaodong Zheng and Meiyi Zheng were involved in the data collection. Weidai Zhang, Zhixiong Cai, and Ronghe Xu conducted the data analysis and wrote the manuscript. All authors were involved in drafting and revising the manuscript.

## Funding

The authors acknowledge that the present research was sponsored by Science and Technology Plan Project of Shantou City (Shantou [2020] No. $5-7$ ), and Strategic Fund for Science and Technology in Guangdong Province (2021-88-07). All funding bodies were not involved in the study design, data collection, analysis and interpretation of data, or writing of the manuscript.

## Data Availability

Raw data supporting the obtained results are available at the corresponding author.

## Declarations

## Ethics approval and consent to participate

All procedures in the NHANES were approved by the National Center for Health Statistics institutional review board, and written informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

## Consent for publication

Not applicable.

## Competing interests

The authors declare no competing interests.
Received: 20 June 2022 / Accepted: 14 May 2023
Published online: 07 June 2023

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