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Functional capacity in adults with hypertension as assessed by the six-minute walk distance test: systematic review

Capacidade funcional de adultos com hipertensão avaliada pelo teste de caminhada de seis minutos: revisão sistemática

Capacidad funcional de adultos con hipertensión evaluada por el test de caminada de seis minutos: revisión sistemática

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ABSTRACT | This study systematically reviewed the six-minute walk test (6MWT) for assessment of functional capacity of adults with hypertension subjected or not to physical rehabilitation, focusing in walked distance (6MWD) and blood pressure. A literature search was conducted in PubMed, SciELO, LILACS, PEDro, Cochrane, Redalyc, and national journals of physiotherapy using the keywords “*hipertensão*” (hypertension) and “*teste de caminhada de seis minutos*” (*six-minute walk test*) without language or period constraints. Six studies were included: one case-control, one clinical trial, two quasi-experimental and two series of cases. Results from cross-sectional studies suggest preservation of the 6MWD in the mild stage of hypertension, whereas significant lower values in the more severe stage of hypertension or in the presence of comorbidities. Longitudinal studies suggest that the 6MWT is sensitive to the increase in functional capacity due to adaptations from physical rehabilitation programs. Two major limitations compromise the external validity of the included studies: samples with specific phenotypes (same sex; same hypertension stage; narrow age group) and the small sample size (range 8 to 32). The low methodological quality reinforces the need for researches with larger samples and different phenotypes of hypertension.

Keywords | Hypertension; Rehabilitation; Review Literature as Topic.

RESUMO | Este trabalho revisou sistematicamente os estudos sobre teste de caminhada de seis minutos (TC6) para avaliação da capacidade funcional de adultos com hipertensão submetidos ou não à reabilitação física, com foco na distância caminhada (DC6) e pressão arterial. Uma busca na literatura foi conduzida no PubMed, SciELO, LILACS, PEDro, Cochrane, Redalyc e em periódicos nacionais de fisioterapia com as palavras-chave “*hipertensão*” (*hypertension*) e “*teste de caminhada de seis minutos*” (*six-minute walk test*) sem restrição de idioma e período. Foram incluídos um estudo caso-controle, um ensaio clínico, dois quase-experimentais e duas séries de casos. Os estudos seccionais sugerem preservação da DC6 nos estágios leves da hipertensão, mas reduções significativas nos estágios mais graves e/ou na presença de comorbidades. Os estudos longitudinais sugerem que o TC6 é sensível ao aumento da capacidade funcional em razão das adaptações oriundas dos programas de reabilitação física. Duas importantes limitações comprometem a validade externa dos estudos incluídos: amostras com fenótipos específicos (mesmo sexo; mesmo estágio de HAS; faixa etária estreita) e pequeno tamanho amostral (entre 8 e 32 participantes). A baixa qualidade metodológica dos estudos reforça a necessidade de pesquisas com amostras maiores e espectro mais amplo de fenótipos de hipertensão.

Descritores | Hipertensão; Reabilitação; Literatura de Revisão como Assunto.

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RESUMEN | Eso trabajo revisó sistemáticamente los estudios referentes al test de caminata de seis minutos (TC6) para evaluación de la capacidad funcional de adultos con hipertensión que fueron o no sometidos a la rehabilitación física, con foco en la distancia caminada (DC6) y en la presión arterial. Una búsqueda en la literatura fue conducida en PubMed, SciELO, LILACS, PEDro, Cochrane, Redalyc y en periódicos brasileños de fisioterapia con las palabras clave "hipertensión" (*hypertension*) y "test de caminata de seis minutos" (*six-minute walking test*) sin restricciones de lengua y periodo. Fueron incluidos uno estudio caso-control, un ensayo clínico, dos casi-experimentales y dos reportos de casos. Los estudios transversales sugieren preservación de la DC6 en los estadios leves de la hipertensión, pero

reducciones significativas en los estadios más severos y/o en la presencia de comorbidades. Los estudios longitudinales sugieren que el TC6 es sensible al aumento de la capacidad funcional porque hay adaptaciones advenidas de programas de rehabilitación física. Dos importantes limitaciones comprometen la validez externa de los estudios: muestras con fenotipos específicos (mismo sexo; mismo estadio de HAS; edad estrecha) y pequeño tamaño de la muestra (entre 8 y 32 participantes). La baja cualidad metodológica de los estudios resalta la necesidad de investigaciones con muestras mayores y espectro más amplio de fenotipos de hipertensión.

Palabras Clave | Hipertensión; Rehabilitación; Literatura de Revisión como Asunto.

INTRODUCTION

The systemic arterial hypertension is a public health issue with a prevalence estimated at 3.3% in 2010, in Brazil¹. High blood pressure increases death risk due to cardiovascular diseases (CDD)² and is associated with blood functional anatomy adjustments that result in injuries of target-organs like heart, kidneys, and brain². Blood remodeling also happens in the musculoskeletal vessels³, which individually compromises its function and globally results in functional limitation of the hypertensive adult⁴. Functional capacity investigation may contribute for comprehending hypertension limitations, as well as for determining the effects of interventions and planning of strategies aimed at preventing disabilities due to injuries in the target-organs.

Among the methods of functional capacity evaluation in hypertensive subjects⁵⁻¹⁰, the six-minute walking test (6MWD) is applied due to its simplicity and easy use^{11,12}. The 6MWD assesses the tolerance to self-limited exercise and is similar to daily life activities (DLAs), therefore it becomes clinically attractive^{9,11,12}. The American Thoracic Society (ATS) established indications, safety measures and procedures to apply the 6MWD¹³. The distance walked during the 6MWD (DW6) is used as a closure for the evaluation of adjustments from physical rehabilitation protocols and for the study of factors associated with functional capacity in absolute values or percentages cited in equations obtained from the healthy population^{13,14}. However, it is not clear if the 6MWD is an indicator of functional incapacity in hypertension and if it captures adjustments performed at physical

rehabilitation programs. Therefore, this paper systematically reviewed studies on the 6MWD to assess the functional capacity of adults with high blood pressure submitted, or not, to physical rehabilitation focused on the 6DW and blood pressure (BP).

METHODOLOGY

A systematic review¹⁵ was conducted in free electronic databases like PubMed, Scielo, LILACS, PEDro, Cochrane and Redalyc using the keywords "hypertension" (*hipertensão*) and "six-minute walking test" (*teste de caminhada de seis minutos*) without language and time constraints. Additional research was conducted in sites of Brazilian journals about physical therapy (*Revista Brasileira de Fisioterapia; Revista Fisioterapia e Pesquisa; Revista Fisioterapia em Movimento*). The last research was done on April 2013 (Figure 1).

Abstracts from the identified articles were examined as to the inclusion criteria: articles (originals), outline (all except review), target population (>18 years old; both genders), diagnosis (systemic arterial hypertension, with or without comorbidities), intervention (none; physical rehabilitation), and observation or intervention outcomes (6DW; systolic and diastolic BP). Double copies between the referred basis and studies about other diseases (e.g. pulmonary arterial hypertension) were excluded.

After completely reading the included studies, the following information were gotten: outline; samples

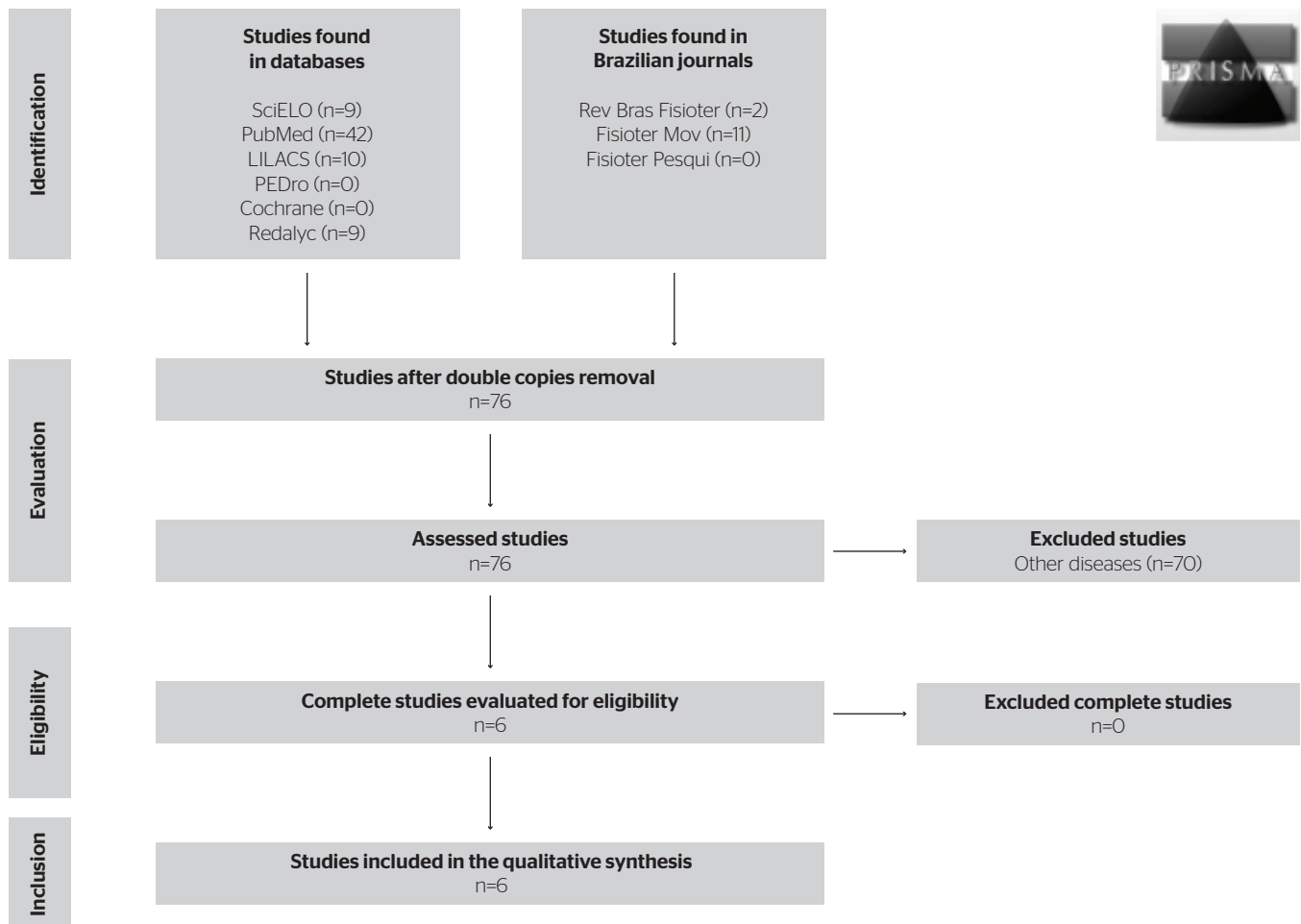


Figure 1. Study flowchart

(case and control groups if applicable); clinical characteristics; systolic and diastolic BP values (baseline and post-intervention if applicable); absolute values of 6DW (in meters); and assumed 6DW values (in the percentages and equations used). Incomplete pieces of information were achieved by mailing the authors, whenever it was possible. Data were typed in an electronic spreadsheet with automatic control of data validation with regard to consistence, which is available upon request to the authors.

The methodological quality of studies was assessed by bias criteria¹⁶: selection, performance, detection, discord, and report. Quality was ranked as low/inaccurate/high risk of bias (low risk: “Yes”; high risk: “No”; other cases: “Inaccurate”). Studies were classified in three levels: low risk of bias (all items = “low risk”), high risk (at least one item = “high risk”) and inaccurate (at least one item = “inaccurate risk”). All procedures were independently performed by two examiners, and disagreements were solved by mutual agreement.

RESULTS

Seventy-six articles were found and six of them were included in this study: one case-control study¹⁷, one clinical essay¹⁸, two quasi-experimental^{19,20}, and two case reports^{21,22} (Table 1). The sample size varied from eight in the clinical essay¹⁸ to 45 subjects in the case-control study¹⁷. Studies analyzed patients grouped per gender, hypertension stage, and/or age range. Most studies followed integrally or partially all recommendations from the ATS¹³ for the 6MWD. Two studies^{18,21} calculated the predicted distance with reference equations for the healthy population²³⁻²⁵. All studies included reported the use of drug therapy for hypertension and good tolerance to the 6MWD, and none of them reported side effects of the 6MWD.

Characteristics of the Studies

Ribeiro *et al.*¹⁷ compared the functional capacity of hypertensive and diabetic (G1), hypertensive (G2) and

Table 1. Studies about functional capacity of hypertensive adults with the six-minute walking test

Study outline	Sample description	Clinical characteristics (Mean±SD)	Blood pressure, mmHg (Mean±SD)	Walked distance, m (Mean±DP ou %)
Case-control ¹⁷	Women, divided into (n=15 each): G1 (hypertension and diabetes); G2 (hypertension); and G3 (healthy)	G1: 61.3±6 years G2: 63.1±4 years G3: 57.3±5 years	SBP/DBP: 132±1/84±8 SBP/DBP: 103±2/88±1 SBP/DBP: 119±7/81±1	G1: 443±5 G2: 468±4 G3: 516±5 p<0.05
Clinical essay (experimental) ¹⁸	Women (n=8), stage I hypertension, sedentary, without comorbidities, under drug therapy, randomly divided into two groups (n=4 each)	G1: 66.5±31 years G2: 57.8±12.3 years	Pre (SBP/DBP): G1: 145±13/88±5 G2: 142±15/88±5 Post (SBP/DBP): G1: 140±8/86±5 G2: 120±12/67±10 p ^A	Pre ^A Post ^A p ^A
Quasi-experimental ¹⁹	Women (n=10), stage I hypertension, sedentary, post-menopause, under drug therapy	56.9±6 years 29.5±6.1 kg/m ²	Pre (SBP/DBP): 143±6/87±5 Post (SBP/DBP): 131±6/82±4 p<0.002	Pre: 511±42 Post: 556±43 p=0.009
Quasi-experimental ²⁰	Hypertensive women (n=10), with comorbidities, under drug therapy	70.7±7.4 years 1.56±0.06 m 61.6±9.04 kg	Pre (SBP/DBP): 150±16/94±8 Post (SBP/DBP): 133±12/77±11 p<0.05 ^B	Pre: 419±59 Post: 436±72 p=0.081
Case reports ²¹	Men (n=10), stage I hypertension, sedentary, non-alcoholics, non-smokers, without comorbidities, without injuries in the target-organs	48.9±5.95 years 1.69±0.05 m 82.2±14.3 kg	SBP: 136.5±18.58 DBP: 87.4±10.59	593±61 103%, p=0.280 ^D 95%, p=0.074 ^E 108%, p=0.022 ^F
Case reports ²²	Hypertensive women (n=32), sedentary, with comorbidities, under drug therapy	65.4±5.4 years 26.1±0.06 kg/m ²	SBP: 134.4±14.9 DBP: 87.0 ^{BC}	428±85

^A Non-presented data. ^B Data reported by the authors. ^C Median. ^D Predicted by Enright and Sherrill²³ equation. ^E Predicted by Troosters *et al.*²⁴ equation. ^F Predicted by Enright *et al.*²⁵ equation. SBP: systolic blood pressure. DBP: diastolic blood pressure

healthy (G3) women. The 6MWD was applied twice according to the ATS¹³ recommendations with one-hour interval between the repetitions. Significantly higher values in the second 6MWD (p<0.05) were seen in all groups. It was observed a significant difference between the three groups (G1<G2<G3; p<0.05). Values of systolic (SBP) and diastolic (DBP) BP and of heart frequency (HF) showed significant increases after the 6MWD (p<0.05), which confirms the characteristics of safety and sub-maximum test.

Accyoli e Piotto¹⁸ analyzed the cardiovascular adaptations induced by a cardiac rehabilitation program in hypertensive sedentary women. Voluntaries were randomly assigned into two groups, and undergone a program conducted in a therapeutic pool (G1) and on the floor (G2) during eight weeks, twice a week, for an hour. 6MWD was performed satisfying ATS requirements¹³. Although the study mentions using a prediction equation²³, the

6DW numerical results and predicted values were not presented. There was a significant decrease in the SBP (p=0.034) and DBP (p=0.020), therefore there may have been a good result of the physical exercise to control BP.

Lima *et al.*¹⁹ investigated the result of a 12-week aerobic training in the functional capacity and in controlling BP of stage I hypertensive, sedentary and going through menopause women. The rehabilitation program consisted of aerobic activity of moderate intensity (warming, stretching, walking, stretching and relaxing) for 50 minutes. 6MWD was performed following ATS protocol¹³. The study showed an increase of the 6DW (p=0.009) after practice period and decrease of BP values (p=0.033), therefore the aerobic training may contribute for hemodynamic and functional improvement.

Souza *et al.*²⁰ analyzed the correlation between functional capacity and quality of life of women who have undergone an enduring and self-stretching training

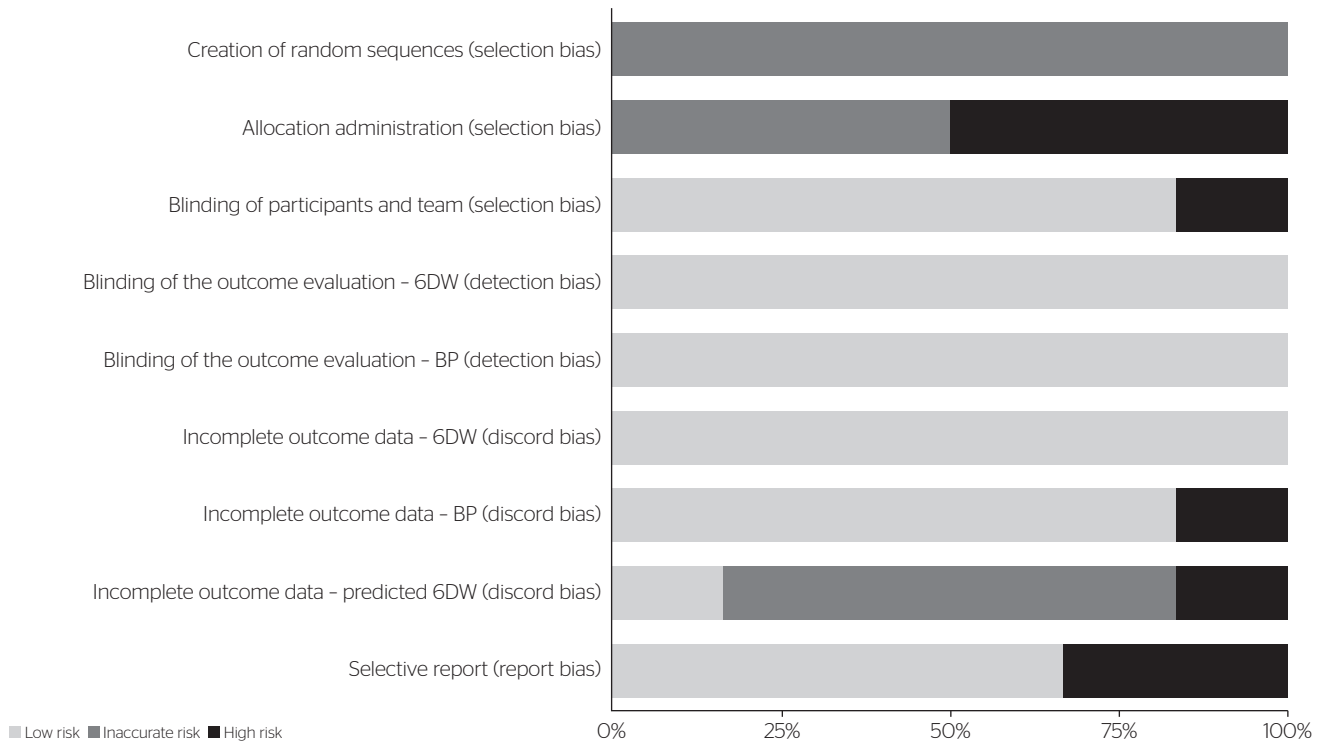


Figure 2. Bias risk in the included studies

program for ten weeks. The women performed the 6MWD according to ATS recommendations¹³, and quality of life was assessed by the SF36 questionnaire. It was seen a decrease of BP values after the training period ($p < 0.05$), but there was no significant increase in the 6DW ($p = 0.081$) nor in the functional capacity domain of the SF36 ($p = 0.72$). Authors suggest a moderate positive correlation between 6DW and SF36 domains that express the functional capacity.

Costa *et al.*²¹ tested the association between BP, perceived effort index (PEI) and 6DW in men at hypertension stage I. The 6MWD was performed according to ATS (2002) and the predicted 6DW was calculated by three equations²³⁻²⁵. Results showed 6DW predicted by Enright *et al.*²⁵ equation significantly overestimated ($p = 0.022$), but there were no significant differences according to other equations^{23,24}.

Pedrosa and Holanda²² tested the correlation between two-minute stationery gait test (2SGT), timed up and go test (TUG) and 6MWD. Aged hypertensive women were assessed without hormonal replacement for menopause. The study did not report if the ATS recommendations were followed¹³. Participants performed three tests with a ten-minute break. All chosen women performed

the tests without interferences. Significant correlations between 6DW and TUG ($r = -0.59$; $p < 0.001$) and between 6DW and 2SGT ($r = -0.66$; $p < 0.001$) suggested a relation between cardiovascular resistance and functional mobility.

Bias risk analysis can be seen in Figure 2. It was seen a high bias risk of selection in the longitudinal studies due to the insufficient or absent randomization description. Other studies present high risk for outcome bias because they do not present all outcome data. The majority of studies presented inaccurate bias risk due to lack of description of methods.

DISCUSSION

This paper systematically reviewed studies about 6MWD to evaluate the functional capacity of adults with high blood pressure who had been or had not been submitted to physical rehabilitation. The sectional studies suggest that in light hypertension stages, there is no significant alteration in the functional capacity as evaluated by the 6MWD²², but significant decreases can be seen in more severe stages and/or in the presence

of comorbidities^{17,22}. On the other hand, longitudinal studies suggest that 6MWD is sensitive to the increase of functional capacity due to the adjustments from physical rehabilitation programs¹⁸⁻²⁰. Two studies^{18,20} calculated the predicted 6DW, but only one²¹ reported the predicted values using international equations²³⁻²⁵. This review also identified the high or inaccurate bias risk in most analyzed criteria.

The high or inaccurate bias risk in the included studies is not uncommon in systematic reviews, but it compromises authors' inferences on the results of the studies alone or collectively²⁶. Two important methodological limitations were common in the reviewed studies and contributed for the bias risk: approach of specific phenotypes (same gender, same hypertension stage, narrow age range) and small sample size. The study of population subgroups is justified due to the group's higher homogenization because of the varied phenotype of hypertension, but it also characterizes an spectrum bias²⁷ that, when combined to the small sample size, limits even more the external validity of these studies. Another interesting point is the identification of only Brazilian studies. Although both the quantity of longitudinal studies and also sectional ones in adults with CDD have been increasing all around the world, most international studies include patients with heart failure (associated or not with hypertension) or pulmonary arterial hypertension^{12,14}, which explains the reduced amount of studies included in the qualitative analysis.

The predicted 6DW was highly overestimated by one²⁵ among three²³⁻²⁵ international equations used in one included study²¹. Brazilian equations of 6DW prediction in a healthy adult population²⁸⁻³⁰ were not available at the time of Costa *et al.*²¹ study, and they should be firstly analyzed in future studies due to the regional differences in 6DW³¹.

It should be emphasized that the development of a systematic review does not overcome the outline problems of the included studies, which is one of their main limitations³². However, following international recommendations¹⁵ for its accomplishment minimize the subjectivity of results and its impact on the interpretations of the included studies³². Given the high prevalence of hypertension in the adult Brazilian population¹ and its association with functional disability⁴, new studies with more representative samples (wide spectrum of phenotypes) should be carried out in order to determine the reference values of 6MWD in hypertensive adults to use in the physical rehabilitation and to find factors associated with 6DW in such population.

CONCLUSIONS

The functional capacity may be decreased in more severe stages of hypertension and/or in the presence of comorbidities. 6MWD seems sensitive to the increase of functional capacity resulting from physical rehabilitation programs in hypertensive patients. Low methodological quality of studies reinforces the need of researches with bigger samples and a wider spectrum of hypertension phenotypes.

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