



ARAŞTIRMA / RESEARCH

Blood pressure limits affecting carotid artery injury: a cross sectional study

Karotis arter hasarını etkileyen kan basıncı sınırları: kesitsel bir çalışma

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Abstract

Purpose: Although it is well known that high blood pressure causes undesirable effects on carotid arteries, it is not clear as to which threshold value this effect starts. The aim of this study is to evaluate and determine this threshold.

Materials and Methods: This cross-sectional study included a total of 308 individuals in the following groups; group 1: individuals with systolic blood pressure (SBP) <120 mmHg and diastolic blood pressure (DBP) <80 mmHg (optimal), group 2: SBP 120-129 mmHg and/or DBP 80-84 mmHg (normal), group 3: SBP 130-139 mmHg and/or DBP 85-89 mmHg (high-normal), group 4: SBP 140-159 mmHg and/or DBP 90-99 mmHg, group 5: SBP 160-179 mmHg and/or DBP 100-109 mmHg, and group 6: SBP≥180 mmHg and/or DBP≥110 mmHg. Carotid distensibility and elasticity were measured in all groups.

Results: A statistically significant difference was determined between the groups in carotid distensibility and elasticity. SBP>135.5 mmHg started to affect carotid distensibility with 78.2% sensitivity and 74.6% specificity, and DBP>86.5 mmHg with 79.3% sensitivity and 71.6% specificity. Carotid elasticity was seen to be affected by SBP>137.5 mmHg with 80.4% sensitivity and 73.1% specificity, and DBP>88.5 mmHg with 79.1% sensitivity and 73.8% specificity.

Conclusion: Carotid distensibility and elasticity decreases with increasing blood pressure. Individuals in high-normal group should be evaluated in terms of carotid disease, and it may be necessary to start treatment early in these patients.

Keywords: Carotid artery injury; Doppler; Hypertension; Elasticity; Distensibility

Öz

Amaç: Yüksek kan basıncının karotis arterler üzerinde istenmeyen etkilere yol açtığı iyi bilinmesine rağmen bu etkinin hangi değerden itibaren başladığı net değildir. Bu çalışmanın amacı karotis arter hastalığının hangi kan basıncı değerinden itibaren başladığını değerlendirmektir.

Gereç ve Yöntem: Çalışma kesitsel planlandı ve toplam 308 birey dahil edildi. Sistolik kan basıncı (SKB) <120 mmHg ve diyastolik kan basıncı (DKB) <90 mmHg olan (optimal) bireyler 1. gruba, SKB 120-129 mmHg ve/veya DKB 80-84 mmHg olan (normal) bireyler 2. gruba, SKB 130-139 mmHg ve/veya DKB 85-89 mmHg olan (yüksek-normal) bireyler 3. gruba, SKB 140-159 mmHg ve/veya DKB 90-99 mmHg olan bireyler 4. gruba, SKB 160-179 mmHg ve/veya DKB 100-109 mmHg olan bireyler 5.gruba ve SKB≥180 mmHg ve/veya DKB≥110 mmHg olan bireyler 6.gruba alındı. Tüm gruplarda karotis distensibilitesi ve elastisitesi ölçüldü.

Bulgular: Tüm gruplar arasında karotis distensibilitesi ve elastisitesi yönünden istatistiksel anlamlı fark vardı. SKB>135,5 mmHg olmasının %78,2 sensitivite, %74,6 spesifite, DKB>86,5 mmHg olmasının %79,3 sensitivite ve %71,6 spesifite ile karotis distensibilitesini etkilemeye başladığı bulundu. Benzer olarak SKB>137,5 mmHg olmasının %80,4 sensitivite, %73,1 spesifite, DKB>88,5 mmHg olmasının ise %79,1 sensitivite ve %73,8 spesifite ile karotis elastisitesini etkilemeye başladığı gösterildi.

Sonuç: Karotis distensibilitesi ve elastisitesi kan basıncının artışı ile azalmaktadır. Yüksek-normal kan basıncına sahip bireyler karotis hastalığı yönünden değerlendirilmelidir ve bu hastalarda tedaviye erken başlamak gerekebilir.

Anahtar kelimeler: Doppler, hipertansiyon, karotis arter hastalığı, elastisite, distensibilite

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INTRODUCTION

Cardiovascular diseases are currently the most important causes of morbidity and mortality worldwide ¹. Atherosclerotic vascular diseases constitute the greatest part of the cardiovascular diseases that cause mortality ¹. Atherosclerosis in the carotid arteries and the resulting cerebrovascular events play an important role in these morbidity and mortality rates. Although many minor risk factors have been identified for atherosclerotic vascular diseases, male gender, diabetes mellitus, dyslipidemia, smoking, hypertension and family history have been identified as the major risk factors ². Among these risk factors, hypertension is important in terms of early recognition and prevention of complications ³. While systolic blood pressure (SBP) ≥ 140 mm Hg and / or diastolic blood pressure (DBP) ≥ 90 mm Hg is defined as hypertension in adults, SBP <120 mm Hg and DBP <80 mm Hg are defined as optimal blood pressure ⁴. The classification of blood pressure and grading of hypertension according to the recently published hypertension guidelines of the European Society of Cardiology. According to this guide, patients were divided into 6 groups; group 1: individuals with SBP <120 mmHg and DBP <80 mmHg (optimal), group 2: SBP 120-129 mmHg and/or DBP 80-84 mmHg (normal), group 3: SBP 130-139 mmHg and/or DBP 85-89 mmHg (high-normal), group 4: SBP 140-159 mmHg and/or DBP 90-99 mmHg, group 5: SBP 160-179 mmHg and/or DBP 100-109 mmHg, and group 6: SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg.

The effect of elevated blood pressure on atherosclerosis in the carotid arteries has been well known for many years. Although many imaging methods can be used to evaluate atherosclerosis in carotid arteries, ultrasonography is frequently used in daily practice because it is cheap, easily accessible and non-invasive. Carotid elasticity and distensibility are two important parameters that can be easily evaluated by ultrasonography and show subclinical atherosclerosis. The role of both elasticity and distensibility in predicting cardiovascular adverse events has been demonstrated in previous studies ⁵⁻⁷.

Although it is well known that high blood pressure causes undesirable effects on carotid arteries, at which value this effect starts is not clear. The aim of this study was to determine this threshold. The patients were separated into 6 different groups

according to the blood pressure values and it was investigated whether there was any difference between these groups in terms of carotid elasticity and distensibility. When a difference was found, it was then investigated from which blood pressure threshold values the distensibility and elasticity started to be affected.

MATERIALS AND METHODS

This cross-sectional study included individuals who presented at the Cardiology Outpatient Clinic of Baskent University, Faculty of Medicine, Adana and İzmir Hospitals and who met the criteria for participation in the study. The age, gender, height, weight and laboratory data of all the study participants were recorded. Ambulatory blood pressure monitoring was performed for 24 hours on all subjects and the 24-hour mean blood pressure values were determined (blood pressure was measured every 30 minutes during the day and once an hour during the night). The participants were separated into 6 groups according to their blood pressure values. Individuals with SBP <120 mm Hg and DBP <90 mm Hg (optimal blood pressure) were placed in group 1, individuals with SBP 120-129 mm Hg and / or DBP 80-84 mm Hg (normal blood pressure) were included in group 2, those with SBP of 130-139 mm Hg and / or DBP of 85-89 mm Hg (high-normal blood pressure) were placed in group 3, those SBP of 140-159 mm Hg and / or DBP individuals with 90-99 mm Hg (grade 1 hypertension) were placed in group 4, those with SBP 160-179 mm Hg and / or DBP 100-109 mm Hg (grade 2 hypertension) were placed in group 5, and those with SBP ≥ 180 mm Hg and / or DBP ≥ 110 mm Hg (grade 3 hypertension) were included in group 6. Any subjects with isolated systolic hypertension, defined as SBP ≥ 140 mm Hg and DBP <90 mm Hg, were excluded. The carotid distensibility and elasticity of all the participants were evaluated and the data were recorded.

After all participants were informed in detail about the purpose of the study, written consent was obtained. This study was approved by Baskent University Institutional Review Board and Ethics Committee (Project no: KA19/339, approval date: 11/20/2019) and supported by Baskent University Research Fund.

The patients were excluded from the study if they had

previously been diagnosed with hypertension (and were therefore using antihypertensive drugs), had any known atherosclerotic cardiovascular disease, diabetes mellitus, dyslipidemia, chronic renal failure, chronic liver disease, vasodilator drug use, known systemic disease, connective tissue disease, hypo or hyperthyroidism, heart failure, advanced heart valve disease, anticoagulant drug use, atrial fibrillation, autoimmune diseases, were smokers, were aged <18 or > 65 years, did not wish to participate in the study, or had a Doppler image of insufficient quality for evaluation.

Evaluation of carotid distensibility and elasticity

Imaging of the carotid arteries was performed according to standard protocols previously determined by the American Society of Echocardiography and Mannheim Consensus Statements⁸⁻⁹. All participants were positioned supine with the head turned to the left at a 45 angle, clearly exposing the right side of the neck. First, the operator visualized the carotid artery both above and below the carotid bifurcation. The probe was then rotated to obtain a longitudinal image of the proximal sections of the common carotid artery and carotid bulb. In this image, the lumen diameter was calculated by measuring the intima-intima distance between the distal and proximal walls.

Minimal vessel diameter (VDmin) was calculated by measuring media-media distance at the end of diastole in 3 consecutive heartbeats. The same measurement was also taken during systole to record maximum vessel diameter (VDmax). The average of 3 measurements was recorded. Participants were monitored by electrocardiogram (ECG) during the

ultrasonographic evaluation and systole and diastole separation was performed according to the ECG.

The formula $[(VD_{max} - VD_{min}) / VD_{min}] \times 100$, described in previous studies, was used to determine carotid artery distensibility (%)¹⁰. Carotid artery elasticity (% / mm Hg) was calculated according to the formula $[(LD_{max} - LD_{min}) / LD_{min}] / \Delta P \times 100\%$, which has been shown to be safe and effective in many studies¹⁰⁻¹². In this formula, ΔP was calculated by taking the difference between systolic and diastolic blood pressure. All measurements for both distensibility and elasticity were made automatically on the software program.

Statistical analysis

For discrete and continuous variables, descriptive statistics (mean, standard deviation, median, minimum value, maximum value, and percentile) were given. In addition, the homogeneity of the variances, which is one of the prerequisites of parametric tests, was checked through Levene's test. The assumption of normality was tested via the Shapiro-Wilk test. To compare the differences between three and more groups, one-way analysis of variance was used when the parametric test prerequisites were fulfilled, and the Kruskal Wallis test was used when such prerequisites were not fulfilled. The Bonferroni correction method, which is a multiple comparison test, was used to evaluate the significant results concerning three and more groups. The cut-off points of the parameters were evaluated by ROC analysis. AUC Value, Sensitivity, Selectivity values were calculated. The data were evaluated via SPSS 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). $p < 0.05$ and $p < 0.01$ were taken as significance levels.

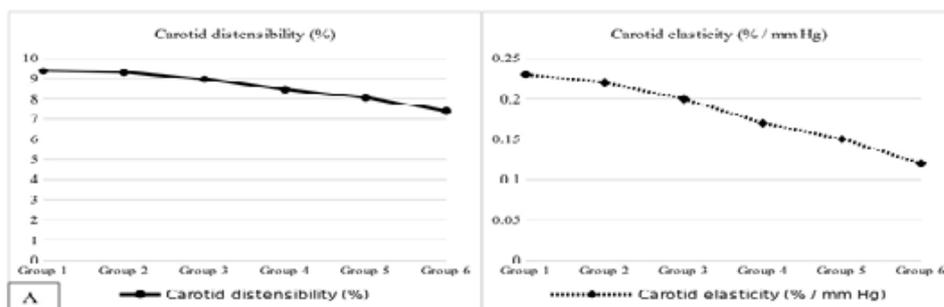


Figure 1. Change of carotid distensibility (A) and elasticity (B) values among the groups

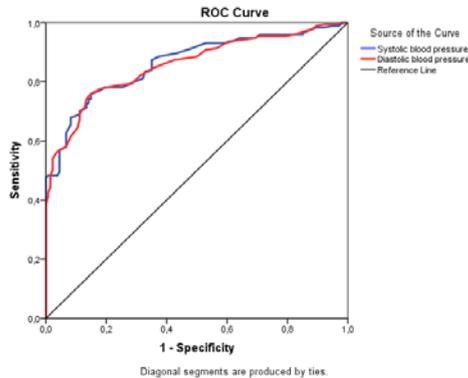


Figure-2. Receiver operating characteristic curve analysis of systolic and diastolic blood pressure for the prediction of carotid distensibility injury.

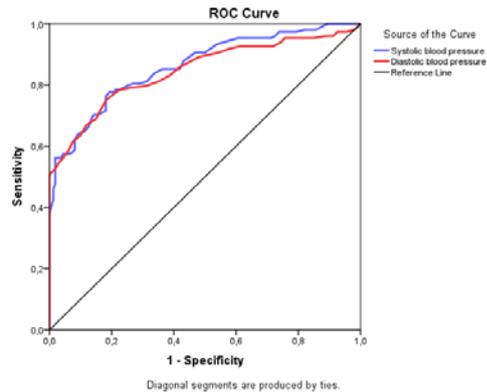


Figure-3. Receiver operating characteristic curve analysis of systolic and diastolic blood pressure for the prediction of carotid elasticity injury.

RESULTS

In this study, a total of 308 individuals were included with 53 in group 1, 51 patients in group 2, 52 in group 3, 52 in group 4, 49 in group 5 and 51 in group 6. There was no statistically significant difference between the groups in terms of baseline demographic and laboratory characteristics ($p > 0.05$). SBP and DBP were significantly different between the groups ($p < 0.05$). The basal demographic characteristics, laboratory values, systolic and diastolic blood pressure values of the 6 groups are shown in Table-1. Carotid distensibility and elasticity were statistically different between the 6 groups ($p < 0.001$). In table-1, the distensibility and elasticity values of all the groups and the comparisons are shown. Figure-1 shows the change in carotid distensibility (A) and elasticity (B) between the groups, respectively.

Receiver operating characteristic (ROC) analysis showed that carotid distensibility was affected by SBP > 135.5 mm Hg with 78.2% sensitivity and 74.6% specificity ROC area under curve [AUC]: 0.863, 95% CI: 0.823–0.904, $p = 0.001$), and SBP > 86.5 mm Hg with sensitivity of 79.3% and specificity of 71.6% (ROC AUC: 0.857, 95% CI: 0.816–0.898, $p = 0.001$) (Figure-2). Carotid elasticity was found to be affected by SBP > 137.5 mm Hg with 80.4% sensitivity and 73.1% specificity (ROC AUC: 0.861, 95% CI: 0.820–0.902, $p = 0.001$), DBP > 88.5 mm Hg with 79.1%

sensitivity and specificity of 73.8% (ROC AUC: 0.845, 95% CI: 0.800–0.891, $p = 0.001$) (Figure-3).

DISCUSSION

The main result of this study was that carotid distensibility and elasticity decrease with increasing blood pressure. In addition, in individuals with high-normal (group 3) blood pressure (SBP 130-139 and / or DBP 85-89 mm Hg), carotid artery damage may be initiated after a certain blood pressure value.

It is well known that hypertension accelerates the development and progression of atherosclerosis. Although this effect cannot be explained clearly, some complex mechanisms may play a role. Blood pressure is a direct exterminator on vascular smooth muscle cells and endothelial cells. As a result, indirect oxidative stress may accelerate this process. In addition, these forces trigger cell proliferation, vascular remodeling, and apoptosis. These results in a strong inflammatory response and all these inflammatory cells, including cytokines are directed to the intima media of the arteries, leading to the formation of atherosclerotic lesions and hardened vessel segments in this region¹³⁻¹⁴.

Although hypertension has been known to be a risk factor for atherosclerosis and unwanted cardiovascular events for many years, it is not clear from which blood pressure threshold value this effect

starts. In the Seventh Report of the National Committee for the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7), published in 2003, SBP of 120-140 mm hg, and DBP between 80-90 mm hg was defined as pre-hypertension¹⁵. In the JNC8 report, which was updated in 2014, this definition was continued, but in both reports it was not clear whether pre-hypertensive patients should be treated, since it was not clear whether pre-hypertension posed a risk to patients¹⁶. There are some data in the literature suggesting that subclinical organ damage has already started in pre-hypertension. In those studies, and meta-analyses, it has been concluded that cardiovascular risks increased at values of >115 mm for SBP and >75 mm Hg for DBP¹⁷. In the current study, these values were found to be slightly higher. This difference may be due to fact that the focus of this study was on assessment of the risk to the carotid, and not the total cardiovascular risk. In addition, different risk factors affecting the development of atherosclerosis may have different effects on different arteries. For example, studies have shown that smoking and diabetes have more impact than other risk factors in the development of femoral atherosclerosis¹⁸. According to the results of the current study, the effect of blood pressure on the development of carotid atherosclerosis may be delayed.

Previous studies of different age groups have shown a parallel increased relationship between carotid intima-media and blood pressure. This may be due to the direct mechanical effect of blood pressure on the arterial wall or the growth effect of some inflammatory cytokines that play a role in the pathophysiology of hypertension on the intima-media. Although excluded from the current study, pre-hypertensive patients are known to have more comorbidities (diabetes mellitus, dyslipidemia, obesity, etc.). All these possible factors may explain the cause of subclinical organ damage in pre-hypertensive patients¹⁸⁻¹⁹.

Ultrasonography is the most commonly used imaging method for evaluating carotid distensibility and elasticity. The main advantages are that it is low cost, easily accessible and non-invasive. Cardiac-phase resolution, which provides high-resolution axial images in carotid arteries, has been used frequently in recent years to assess elasticity and distensibility in magnetic resonance imaging. The major disadvantage of both elasticity and distensibility is that different

methods have been defined for measurements and standard reference values have not been determined. However, there are sufficient reports in the literature to assure that these values reflect atherosclerosis and cardiovascular events²⁰.

Limitations of the study: As this study was cross-sectional, it is not known how the cardiovascular risks will develop in these individuals during long-term follow-up. Another limitation was that carotid elasticity and distensibility provides information about cardiovascular risks in an indirect manner and not through direct means. Another limitation was that there is no standardized reference value in the literature for both measurements and there are many different measurement techniques. An additional limitation was that the evaluation was performed with ultrasonography, which is an operator-dependent method with low reproducibility. The number of patients in each group may be considered relatively low, and further studies with a larger number of patients are required confirmation of these results. Although 24-hour ambulatory blood pressure measurement was used to standardize blood pressure measurement, individuals may have been affected by daily blood pressure changes.

In conclusion, carotid distensibility and elasticity decreases with increasing blood pressure. Individuals in high-normal group should be evaluated in terms of carotid disease, and it may be necessary to start treatment early in these patients.

Yazar Katkıları: Çalışma konsepti/Tasanım: AG, ÇY; Veri toplama: ÇY, MY, EG; Veri analizi ve yorumlama: MAT; Yazı taslağı: AG; İçerğin eleştirel incelenmesi: ÖA; Son onay ve sorumluluk: AG, MY, CA, EG, MAT, ÇY, ÖA; Teknik ve malzeme desteği: MY, EG; Süpervizyon: ÖA; Fon sağlama (mevcut ise): yok.

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