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Original Article

Augmentation Index as a Marker of Vascular Recovery After Endovascular Therapy in Peripheral Artery Disease

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Abstract

Objective: The objective of the study was to evaluate early changes in the aortic augmentation index (AIX) standardized to 75 bpm following successful peripheral endovascular revascularization in patients with peripheral artery disease (PAD).

Methods: This was a single-center, retrospective observational study. AIX was measured at baseline (pre-procedure), 24 h, and 1 month after the procedure using radial applanation tonometry (SphygmoCor®) under standardized conditions. Time effect was assessed with repeated-measures Analysis of Variance (ANOVA) (Greenhouse–Geisser correction if needed) and a linear mixed-effects model (random intercept for patient). Pairwise comparisons (pre–24 h, pre–1 mo, 24 h–1 mo) were adjusted by Holm; Cohen's dz was reported as effect size.

Results: Thirty-seven patients were analyzed. Mean AIX values were 30.6 (pre), 21.4 (24 h), and 21.1 (1 month). The time effect was significant (Repeated Measures ANOVA, $p<0.001$). In the mixed model (pre as reference), AIX decreased at 24 h ($\beta=-9.243\pm1.256$, $p<0.001$) and at 1 month ($\beta=-9.459\pm1.256$, $p<0.001$). Pairwise contrasts confirmed significant reductions from baseline to 24 h and to 1 month, but not between 24 h and 1 month.

Conclusion: Peripheral revascularization is associated with a rapid and sustained reduction in AIX, with most of the improvement achieved within 24 h and maintained at 1 month, suggesting early favorable changes in wave reflection and arterial stiffness.

Keywords: Peripheral arterial disease; pulse wave analysis; vascular stiffness.

Periferik Arter Hastalığında Endovasküler Tedavi Sonrası Vasküler İyileşmenin Bir Göstergesi Olarak Augmentasyon İndeksi

Özet

Amaç: Periferik arter hastalığı (PAH) olan hastalarda başarılı endovasküler revaskülarizasyon sonrası aortik augmentasyon indeksindeki (AİX) erken dönemdeki değişiklikleri değerlendirmek.

Yöntem: Tek merkezli, retrospektif gözlemsel bir çalışmadır. AİX ölçümleri standart koşullarda radial applanasyon tonometrisi (SphygmoCor®) ile işlem öncesi, 24. saat ve 1. ayda yapıldı. Zamanın etkisi tekrarlı ölçümlü ANOVA (gerektiğinde Greenhouse–Geisser düzeltmesi) ve rastgele kesişimli lineer karma etkili model ile analiz edildi. İkili karşılaştırmalar için Holm düzeltmesi uygulandı, etki büyüklüğü Cohen's dz ile raporlandı.

Bulgular: Analize 37 hasta dahil edildi. Ortalama AİX değerleri 30,6 (pre), 21,4 (24. saat) ve 21,1 (1. ay) bulundu. Zamanlama etkisi anlamlıydı (RM-ANOVA, $p<0,001$). Karma modelde AİX, işlem sonrası 24. saatte ve 1. ayda anlamlı şekilde azaldı. Çiftli karşılaştırmalar pre→24 h ve pre→1 ay için anlamlıydı; 24 h→1 ay farkı anlamsızdı.

Sonuç: Periferik revaskülarizasyon, AİX üzerinde erken ve kalıcı bir azalma ile ilişkilidir. İyileşmenin büyük kısmı ilk 24 saatte gerçekleşmekte ve 1. ayda korunmaktadır; bu durum dalga yansıması ve arteriyel sertlik parametrelerinde erken dönemde olumlu değişiklikleri düşündürmektedir.

Anahtar sözcükler: Periferik arter hastalığı; dalga yansıması; damar sertliği.

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Introduction

Peripheral artery disease (PAD) is a condition characterized by atherosclerotic blockages of the arteries beyond the aortic bifurcation. The clinical signs of PAD greatly diminish a person's quality of life. These signs mainly include intermittent claudication, arterial ulcers, necrosis, and in severe cases, gangrene.

The first change in PAD relates to stenosis in the arterial lumen diameter. The severity of arterial stenosis can be non-invasively assessed by ankle-brachial index (ABI). The second change in PAD involves alterations in the viscoelastic properties of the arterial walls. Increased vascular stiffness has been observed in patients with PAD, and this can be evaluated noninvasively using pulse wave analysis (PWA).

Pulse Wave Analysis (PWA)

Augmentation ındex (AIX), derived from PWA, measures the reflected wave's contribution to systolic pressure: AIX = ([P2−P1])/PP)×100 (P1: early systolic forward peak; P2: late systolic reflected peak). AIX is negative when P2<P1 and positive when P2>P1, usually with higher peripheral resistance. In addition to arterial elasticity, total peripheral resistance also influences AIX – lower resistance results in lower AIX. In PAD, resistance is increased and decreases after revascularization. Our study examined how successful percutaneous revascularization impacts aortic AIX in PAD patients.

Materials and Methods

The study was conducted at the Department of Cardiology, Koşuyolu Training and Research Hospital, Istanbul, Turkey, as a single-center, retrospective, observational design. Consecutive adult patients scheduled for endovascular revascularization with a diagnosis of PAD were evaluated. The number of patients included in the final analysis and the sample flow are reported in the Results section. The study was approved by the institutional ethics committee (Decision No: 2017/6/29), and the requirement for individual informed consent was waived due to the retrospective design. The study follows the principles outlined in the Declaration of Helsinki.

Inclusion Criteria

- ≥18 years of age,
- PAD confirmed by clinical and/or imaging,
- Plan for peripheral endovascular revascularization (angioplasty ± stenting),
- Hemodynamic stability Single-center, retrospective, observational study conducted in the Department of Cardiology. Suitable for AIX measurement at pre-procedural and post-procedural time points.

Exclusion Criteria

Congestive heart failure; atrial fibrillation or significant tachyarrhythmias; uncontrolled hypertension (≥180/100 mmHg); advanced renal failure (creatinine >2.0 mg/dL) or dialysis; active infection/sepsis; recent acute coronary syndrome within the last 2 months; significant valvular heart disease; history of chronic obstructive pulmonary disease, chronic bronchitis, pulmonary embolism, or primary pulmonary hypertension; congenital heart disease; isolated right heart failure; previous lower extremity amputation; thyroid dysfunction; malignancy; re-revascularization, major amputation, or death within the 1st month after the procedure; inability to provide informed consent.

Percutaneous transluminal angioplasty (with stenting when needed) was performed using standard techniques based on the lesion site and anatomy. Procedure details (lesion segment, device use, technical success, procedure time, contrast volume) were recorded from the patient file. Post-procedural medical therapy (antiplatelet, statin, antihypertensive, etc.) was managed according to clinical guidelines.

AIX Measurement

Radial artery applanation tonometry was performed using the SphygmoCor®XCEL (AtCor Medical, Sydney, Australia) system; the central (aortic) pressure waveform was obtained through the transfer function. AIX represents the contribution of the late systolic reflected wave to the systolic pressure and is calculated as AIX = ([P2−P1]/PP)×100, where P1 denotes the forward systolic peak, and P2 represents the reflected wave peak. AIX was calculated as the contribution of the reflected wave to the systolic peak and was adjusted to 75 beats/min (AIX@75) to minimize heart rate dependence. Measurements were taken in the morning after fasting, in a quiet environment at 22–24 C, following at least 5 min of rest in a supine position. A quality index of ≥80% was required for the measurements; low-quality recordings were repeated and corrected. AIX values that had been measured at baseline, 24 h, and 1 month after the procedure were retrieved from patient records. Office blood pressure, heart rate, and any medication changes were recorded at each visit.

Demographic data (age, sex), clinical information (hypertension, diabetes mellitus, smoking, comorbidities), treatment details (statin/antithrombotic/antihypertensive), hemodynamic measures (office blood pressure, heart rate), and procedural data (lesion location, device/technical details, complications) were recorded in an electronic form. The time intervals between measurements were checked to ensure protocol adherence. Segments with artifacts or rhythm disorders in AIX recordings were re-measured. Individuals missing measurements at any time point were excluded from the repeated measures analysis for a complete observation approach; however, their available data contributed to the mixed-effects model. Outliers were reviewed based on clinical context and recording quality. Statistical analyses were conducted using IBM the Statistical Package for the Social Sciences Statistics 26.0 (IBM Corp., Armonk, NY, USA) and Python 3.9 (Python Software Foundation, Wilmington, DE, USA) with StatsModels and SciPy packages. The study report adhered to the ICMJE and Koşuyolu Heart Journal guidelines.

Table 1. Demographic characteristics of patients

Variable	Percentage or Mean±SD
Age (Mean±SD)	62.5±11.4
Sex	Male: 86.5%, Female: 13.5%
Smoking status	Smokers: 64.9%, Non-smokers: 35.1%
Hypertension	Hypertensive: 67.6%, Normotensive: 32.4%
Diabetes mellitus	Diabetic: 45.9%, Non-diabetic: 54.1%
CAD	With CAD: 48.6%, Without CAD: 51.4%
CKD	With CKD: 18.9%, Without CKD: 81.1%
CVD	With CVD: 5.4%, Without CVD: 94.6%
Wound presence	With Wound: 32.4%, Without Wound: 67.6%

This table summarizes the demographic and clinical characteristics of the study population. The cohort mainly consisted of older men with a high prevalence of hypertension, diabetes, and smoking, reflecting the typical risk profile of peripheral artery disease. CAD: Coronary artery disease; CKD: Chronic kidney disease; CVD: Cerebral vessel disease; SD: Standard deviation.

Statistical Analysis

(I) Pre-procedure, (II) 24-h, and (III) 1-month follow-ups. Office blood pressure was used to assess the time-dependent change in AIX. Repeated Measures Analysis of Variance (RM-ANOVA) (with Greenhouse–Geisser correction if necessary) and the linear mixed-effects model (LMM), which accounted for individual variation, were used sequentially; the reference level was pre. Paired t-tests were performed to detect differences between time points; the Holm method was used for multiple comparison correction. Results are reported with p-values and Cohen's dz. Numerical details are in Tables 1 and 2, and visual trends are in Figures 1 and 2.

Results

A total of 37 patients were included in the study. The average age of the participants was 62.5±11.4 years, and 86.5% were male.

Table 2. Mean AIX values and paired comparison (Categorical p-values)

Time point	AIX (Mean±SD)	p value vs. previous
Pre-procedure	30.6±11.0	Reference
24 h after procedure	21.4±8.3	p<0.001
1 month after procedure	21.1±7.4	p<0.001

This table shows mean AIX values before and after endovascular therapy. A significant reduction was seen within 24 h and persisted at 1 month, indicating an early and sustained improvement in arterial stiffness. AIX: Augmentation index; SD: Standard deviation.

The prevalence of hypertension was 67.6%, diabetes 45.9%, and a history of smoking 64.9%. These basic demographic and clinical data are summarized in Table 1. In addition, AIX values that had been measured before the procedure (pre), at 24 h, and at 1 month were retrieved from patient records. The mean AIX values were 30.6 pre-procedure, 21.4 at 24 h, and 21.1 at 1 month, indicating a significant early decrease (Table 2). The repeated-measures ANOVA examining the main effect of time found a significant effect of the time factor on AIX (Pr>F<0.001). Therefore, it was confirmed that AIX systematically decreased over time following revascularization. The findings were consistent in the mixed-effects (LMM) analysis, which accounted for individual differences, with pre as the reference point in the model.

- Pre → 24 h coefficient: β=−9.243±1.256, z=-7.359, p<0.001, 95% confidence interval (CI) −11.705 to -6.781.
- Pre→1 month coefficient: β=−9.459±1.256, z=-7.531, p<0.001, 95% CI −11.921 to -6.997.

This indicates that the observed decrease in AIX remained significant even after controlling for patient-level variance. When paired comparisons between time points were evaluated with the Holm correction:

- Pre→24 h: mean difference −9.24 (95% CI −12.26 to -6.22), p(Holm) =7.38×10−7, Cohen's dz=-1.02.

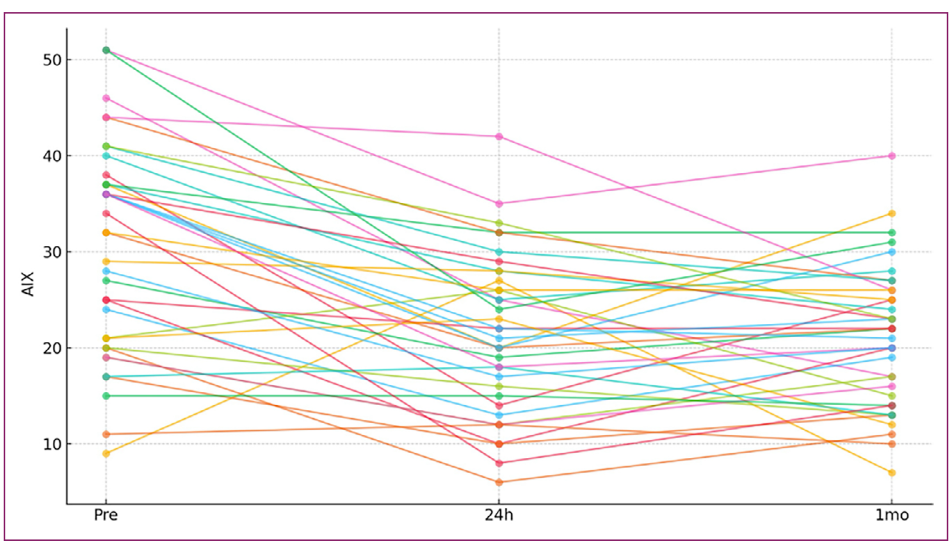

Figure 1. Individual change curves of augmentation index (AIX) over time. The graph shows AIX values at baseline, 24 h, and 1 month. Most patients showed a clear reduction within the first 24 h, and this decrease persisted at 1 (mo).

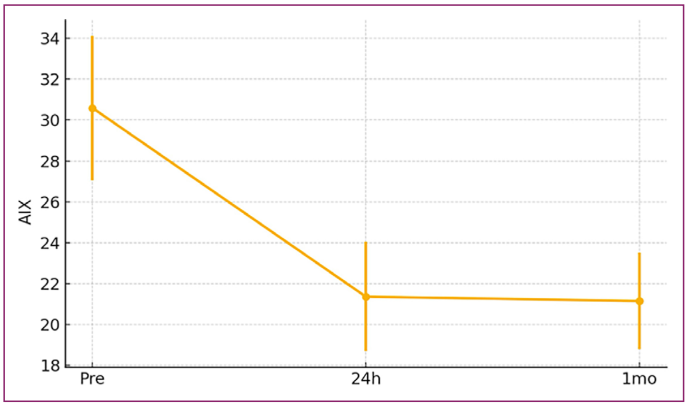

Figure 2. Mean augmentation index (AIX) trends over time with 95% confidence intervals (CIs). This figure shows mean AIX values with 95% CIs. A clear reduction was seen at 24 h and was maintained at 1 (mo), with no significant difference between these time points.

- Pre→1 month: mean difference −9.46 (95% CI −11.65 to −7.27), p(Holm) = 5.65×10−10, Cohen's dz=-1.44.
- 24 h→1 month: mean difference -0.22 (95% CI -2.68 to 2.25), p(Holm) = 0.860, Cohen's dz=-0.03.

Accordingly, the most notable and clinically important decrease occurs from pre to both 24 h and 1 month; the additional change between 24 h and 1 month is not statistically significant. In summary, most of the improvement had already occurred within the first 24 h, and this gain is maintained at 1 month. For a visual summary of the findings, the retrospective analysis of available patient data (Fig. 1) and the mean ±95% confidence interval graph (Fig. 2) show an early and significant reduction consistent with the numerical trend above.

Discussion

Our study demonstrates that successful percutaneous revascularization in patients with PAD significantly reduces the AIX. The initial stage of hemodynamic impairment in PAD is associated with stenosis in the arterial lumen, which can be monitored clinically using a non-invasive indicator called the ABI. The second stage involves changes in the viscoelastic properties of the arterial wall, measurable through PWA. AIX, derived from PWA, is a comprehensive measure reflecting systemic arterial stiffness and wave reflection components. Literature indicates that AIX is elevated in lower extremity arterial disease; however, the mechanisms behind AIX elevation in PAD are not fully understood.[1] Key factors influencing AIX include the arterial tone at reflection sites and the timing of reflections, which are determined by the stiffness of the aorta and large arteries. Endothelial dysfunction, considered an early stage of atherogenesis, has been linked to increased wave reflection.[1] Successful revascularization improves perfusion in the treated limb and often results in increased ABI; higher ABI levels are inversely associated with cardiovascular mortality.[2] Conversely, the effects of peripheral interventions on systemic vascular function markers have been less explored. In PAD, recurrent muscle ischemia promotes a local cycle of inflammation and oxidative stress, characterized by free radical production, neutrophil activation, and endothelial damage.[1] Studies linking walking distance with arterial stiffness suggest that patients with high AIX may have reduced functional capacity.[3] An increased pain-free walking distance after revascularization can promote endothelial health by encouraging physical activity.[4] Reduced ischemia and reactive oxygen species may also increase nitric oxide (NO) bioavailability, a key mediator of arterial compliance.[5] Our study did not directly measure physical activity or NO levels, but previous research shows that flow-mediated dilation improves after lower extremity revascularization.[6] In addition, pharmacological interventions such as flavonoid supplements have been shown to reduce wave reflection and improve endothelial function.[7] Based on this data, it is reasonable to suggest that decreases in AIX following revascularization may be related to improvements in endothelial mediators, especially NO. Geometrical factors such as reflection site location and vessel branching may also contribute to the observed AIX reduction. Arterial stiffness, the size and location of obstructions, the distal vascular network (arterioles), and the arrangement and number of reflection sites all affect reflection timing and amplitude.[8] Experimental and clinical studies show that peripheral stenoses can amplify early wave reflection. For example, in PAD patients with occlusive lesions in the lower extremities, the terminal aorta and/or occluded segment may serve as a reflection source, supporting the idea of "shortening of the effective arterial system length" and a decrease in reflection return time (Tr).[8] Human studies indicate that temporary occlusion of iliac arteries increases aortic reflection, and significant pressure reflection is observed from the occluded segment in severe aortoiliac disease.[9] Therefore, resolving peripheral obstructions may help decrease AIX by causing reflected waves to return later. The key clinical insight is that revascularization, indicated by decreased AIX alongside increased ABI, not only improves local perfusion but also reduces systemic hemodynamic load – specifically, early reflection and afterload. This highlights the potential value of investigating additional prognostic markers, such as AIX (preferably AIX), for risk assessment and follow-up in PAD patients. Given the retrospective nature of the study, causality between revascularization and AIX reduction should be interpreted with caution.

Study Limitations

This study has some limitations that should be acknowledged. First, although the discussion section mentions the ankle-brachial index (ABI), a widely accepted marker for PAD severity and prognosis, ABI measurements were not included in our study. This omission limits the ability to correlate AIX changes with established diagnostic and prognostic parameters in PAD. Second, the sample size is relatively small and was collected from a single center, which may restrict the generalizability of our results. Furthermore, the absence of a control group hinders the attribution of observed changes exclusively to the intervention, as confounding factors such as natural disease progression or placebo effects cannot be excluded. Although AIX is a useful surrogate marker of arterial stiffness and wave reflection, it can be affected by various factors, including heart rate and blood pressure fluctuations. In our study, the use of antihypertensive and cardiovascular medications was consistent across all patients, likely reducing pharmacological interactions. Finally, the one-month follow-up period may be too brief to assess long-term vascular changes or the risk of restenosis, especially in patients with advanced or extensive vascular disease. Future research should include ABI measurements, investigate the relationship between changes in AIX and ABI, and extend follow-up periods. Multicenter, prospective controlled trials are warranted to validate and extend these findings.

Conclusion

Following endovascular therapy in patients with PAD, there was a noticeable early reduction in AIX values. These findings suggest a positive short-term impact on arterial stiffness. Larger-scale and long-term prospective studies are necessary to validate these findings and evaluate their clinical significance.

Disclosures

Ethics Committee Approval: The study was approved by the Koşuyolu Training and Research Hospital Ethics Committee (no: 2017/6/29, date: 23/08/2017).

Informed Consent: Written informed consent was obtained.

Conflict of Interest Statement: None declared.

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