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Romatoid Artritli Hastalarda Arteriyel Sertlik ile Kapilleroskopik Bulgular Arasındaki İlişkinin Değerlendirilmesi

Evaluation of the Correlation Between Arterial Stiffness and Capillaroscopic Findings in Patients with Rheumatoid Arthritis

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ÖZ

Giriş: Bu çalışmanın amacı, romatoid artrit (RA) hastalarında arteriyel sertlik parametreleri ile kapillaroskopik bulgular arasındaki ilişkiyi araştırmak ve bu yöntemlerin kardiyovasküler riske katkıda bulunabilecek subklinik vasküler değişikliklerin tespitindeki potansiyelini incelemektir.

Yöntem: Prospektif olarak planlanan çalışmaya 90 romatoid artritli (RA) hasta ile 90 sağlıklı gönüllü dahil edildi. Tüm katılımcıların yaş, cinsiyet, beden kitle indeksi (VKİ), hastalık süresi, anti-CCP, romatoid faktör (RF), ESR, CRP gibi laboratuvar parametreleri kaydedildi. Arteriyel sertlik parametreleri olarak nabız dalga hızı (PWV), augmentasyon indeksi (AIx75), yansıtma büyüklüğü, çevresel direnç ve nabız basıncı osilometrik yöntemle ölçüldü. Ayrıca eş zamanlı olarak tırnak yatağı video kapilleroskopisi (NVC) uygulanarak kapiller morfoloji ve mikrovasküler değişiklikler değerlendirildi. Ölçümler standart koşullarda ve istirahat durumunda gerçekleştirildi.

Bulgular: RA hastalarında PWV (7,39±1,56 m/sn vs. 6,07±0,89 m/sn; p<0,001), AIx75 (%28,18±9,21 vs. %25,40±9,55; p=0,048), yansıtma büyüklüğü (%60,35±8,18 vs. %57,56±9,92; p=0,014) ve çevresel direnç (1687,7±169,9 dyn·s/cm vs. 1619,9±184,1 dyn·s/cm; p=0,011) kontrol grubuna göre anlamlı derecede yüksek bulundu. Düzenli kapiller ektazi (%47,8 vs. %24,4; p=0,001), tortioze kapiller (%78,7 vs. %48,9; p<0,001), filiform uzamış kapiller (%40,0 vs. %15,6; p<0,001) ve neoanjiogenez (%56,7 vs. %31,1; p=0,001) oranları RA grubunda kontrol grubuna kıyasla anlamlı olarak daha yüksekti. Mikrohemoraji pozitif hastalarda PWV [8,7 (6,4–9,7) vs. 6,9 (5–11,7); p=0,048] ve nabız basıncı [56 (31–63) vs. 42 (18–73); p=0,004] anlamlı şekilde yüksekti. Seropozitif hastalarda çevresel direnç anlamlı şekilde yüksek, nabız basıncı ise düşüktü (p<0.05).

Sonuç: Bulgularımız, RA hastalarında mikrovasküler değişiklikler ile arteriyel sertlik arasında önemli bir ilişki olduğunu göstermektedir ve kapilleroskopi ve arteriyel sertlik parametrelerinin birlikte değerlendirilmesinin, subklinik vasküler değişiklikleri tespit etmeye yardımcı olabileceğini düşündürmektedir.

Anahtar Kelimeler: romatoid artrit, arter sertliği, nabız dalga hızı, kapilleroskopi, kardiyovasküler risk

ABSTRACT

Objective: This study aimed to investigate the relationship between arterial stiffness parameters and capillaroscopic findings in patients with rheumatoid arthritis (RA) and to explore the potential of these methods in detecting subclinical vascular changes that may contribute to cardiovascular risk.

Method: This prospective study included 90 patients diagnosed with rheumatoid arthritis (RA) and 90 healthy controls. Demographic and clinical data, including age, gender, body mass index (BMI), disease duration, and current medication use, were recorded. Arterial stiffness parameters such as pulse wave velocity (PWV), augmentation index (AIx75), reflection magnitude, peripheral resistance, and pulse pressure were measured using an oscillometric method. Simultaneously, nailfold video capillaroscopy (NVC) was performed to evaluate capillary morphology, density, and microvascular architecture.

Results: PWV (7.39±1.56 m/s vs. 6.07±0.89 m/s; p<0.001), AIx75 (28.18±9.21% vs. 25.40±9.55%; p=0.048), reflection magnitude (60.35±8.18% vs. 57.56±9.92%; p=0.014), and peripheral resistance (1687.7±169.9 dyn·s/cm vs. 1619.9±184.1 dyn·s/cm; p=0.011) were significantly higher in RA patients compared to controls. RA patients also had significantly higher positivity rates of regular capillary ectasia (47.8% vs. 24.4%; p=0.001), tortuous capillaries (78.7% vs. 48.9%; p<0.001), filiform elongated capillaries (40.0% vs. 15.6%; p<0.001), and neoangiogenesis (56.7% vs. 31.1%; p=0.001). Additionally, patients with positive microhemorrhage showed significantly higher PWV [8.7 vs. 6.9; p=0.048] and pulse pressure [56 vs. 42; p=0.004]. Seropositive patients showed significantly higher peripheral resistance and lower pulse pressure values (p<0.05).

Conclusion: Our findings indicate a notable association between microvascular changes and arterial stiffness in RA patients, suggesting that combined evaluation of capillaroscopy and arterial stiffness parameters may help detect subclinical vascular alterations.

Keywords: rheumatoid arthritis, arterial stiffness, pulse wave velocity, capillaroscopy, cardiovascular risk

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INTRODUCTION

Rheumatoid arthritis (RA) is the most common inflammatory arthritis characterized by elevated inflammatory markers, joint destruction, and potential multisystem involvement. Patients with RA have mortality rates more than twice those of the general population, predominantly due to cardiovascular diseases. (1)

Chronic inflammation observed in RA patients predisposes them to endothelial dysfunction and increased arterial stiffness, both significant markers of subclinical atherosclerosis and elevated cardiovascular risk. (2, 3) Atherosclerosis increases the stiffness of large arteries, and increased carotid intima-media thickness (IMT) represents one of the earliest detectable stages, predicting plaque development. Age and disease duration are among the most critical factors influencing arterial stiffness. (4, 5)

Arterial stiffness, defined as reduced elasticity of arterial walls, predicts cardiovascular events and is one of the earliest detectable indicators of adverse structural and functional changes in vascular walls. (6) Pulse wave velocity (PWV) and augmentation index (AIx) are reliable methods for assessing arterial stiffness. (7) Increased arterial stiffness is associated with atherosclerosis, increased vascular fibrosis, loss of elastic fibers, and widespread vascular calcification, making it a valuable tool for screening preclinical cardiovascular diseases. (8) Among various non-invasive methods used to measure arterial stiffness, (8) PWV assessment is the most accurate and represents the gold standard among various non-invasive methods used to measure arterial stiffness. (9)

Microvascular changes are among the earliest detectable features in many inflammatory diseases, including RA. (10) Nailfold videocapillaroscopy (NVC) is an easy, reliable, and safe method for assessing peripheral microangiopathy. RA is known to affect the morphology and structure of the microvascular circulation. (11, 12) Therefore, capillaroscopy represents a useful technique for analyzing microcirculation in RA patients, potentially aiding diagnosis, monitoring disease progression, and evaluating treatment response.

In this study, we aimed to determine normal values for PWV, AIx, and capillaroscopic findings in a healthy adult population and to compare these parameters with rheumatoid arthritis (RA) patients. We evaluated arterial stiffness using oscillometric pulse wave analysis (PWA), assessed nailfold capillary changes through simultaneous NVC, and investigated potential correlations between these parameters to enhance early cardiovascular risk prediction in RA patients.

MATERIALS AND METHODS

Study Design

This prospective study was conducted at Gaziantep University Şahinbey Research and Training Hospital between February 2023 and May 2023. Ethical approval was obtained from the Gaziantep University Faculty of Medicine non-invasive clinical research ethics committee (Approval number: 2022/452, Date: 01.02.2023). The study included 90 patients diagnosed with rheumatoid arthritis (RA) and 90 healthy volunteers. The control group consisted of 90 healthy volunteers who were age- and gender-matched to the RA patients using a 1:1 matching strategy. Matching was performed manually during the recruitment process to ensure that each RA patient had a corresponding control within ±3 years of age and the same gender. This approach aimed to reduce the potential confounding effects of age and gender on vascular parameters and improve the comparability between groups. An equal group size was chosen to maintain statistical power and analytical balance in between-group comparisons.

Patients diagnosed with rheumatoid arthritis (RA) and healthy control subjects aged between 18 and 75 years who provided informed consent were included in the study. RA patients were recruited from the Rheumatology Department of Gaziantep University Şahinbey Research and Training Hospital. Participants with cardiovascular diseases, chronic kidney disease, diabetes mellitus, hypertension, hyperlipidemia, active infections, history of premature cardiovascular disease in the family, other rheumatologic diseases, or smoking status were excluded from both patient and control groups based on clinical examination and medical history.

Study Protocol

Participants meeting inclusion and exclusion criteria were enrolled in the study. Data collected included age, gender, height, weight, body mass index (BMI), disease duration, biological agent therapy, anti-CCP, rheumatoid factor (RF), pulse rate, pulse pressure, pulse wave velocity (PWV), augmentation index (AIx75), peripheral resistance, reflection magnitude, troponin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, globulin, uric acid, and capillaroscopic findings (microvascular architecture, capillary distribution, capillary morphology, capillary density, efferent/afferent limb ratio, subpapillary plexus). All data were recorded on standardized data collection forms.

Before capillaroscopy and arterial stiffness measurements, the room temperature was adjusted to 20–22 °C, and subjects were rested for 15 minutes in a seated position to minimize the influence of physical activity, stress, or external factors. Capillaroscopy examination was performed in a seated position using a Dino-lite Digital Microscope, applying immersion oil on the nail bed.

Arterial stiffness measurements were performed using the Mobil-O-Graph NG® 24h PWA device (IEM GmbH, Stolberg, Germany), which employs an oscillometric technique with a standard brachial cuff to estimate central hemodynamic parameters. The device records brachial pressure waveforms and utilizes a validated transfer function to calculate central systolic pressure, pulse pressure, augmentation index corrected to a heart rate of 75 bpm (AIx75), and PWV. Specifically, brachial-based PWV was assessed, reflecting central arterial stiffness. Participants were seated and rested for at least 15 minutes in a temperature-controlled room (20–22°C) before measurement. Four sequential readings were obtained at 5-minute intervals, with the first reading used for calibration and the remaining three averaged to enhance accuracy.

To ensure data quality and reduce measurement variability, the same trained operator conducted all measurements, and cuff positioning was standardized across participants. The validity and reliability of the Mobil-O-Graph device for central arterial stiffness assessment have been demonstrated in prior studies involving hypertensive and inflammatory cohorts. (13, 14) Although it has not been specifically validated in RA

populations, its non-invasive and reproducible properties support its utility in clinical and research settings involving systemic inflammatory diseases.

Capillaroscopy Evaluation Criteria:

- Normal Pattern: Homogeneous capillary distribution without capillary loss or morphological abnormalities.
- Giant Capillaries: Symmetrical dilatations exceeding 50 μm in diameter.
- Microhemorrhage: Presence of at least three pinpoint or linear microhemorrhages per finger, indicating red blood cell extravasation due to vessel wall damage.
- Neoangiogenesis: Clusters of twisted capillary loops, characterized by significantly disrupted homogeneity and variable thin and thick capillary segments.
- Tortuous Capillaries: Capillaries exhibiting abnormal looping and increased tortuosity.
- Capillary Loss (Avascular Areas): Regions with widespread capillary loss (<30 loops within 5 mm in the distal nail bed).
- Meandering (Crossed) Capillaries: Capillaries showing abnormal morphology characterized by two or more crossings.
- Regular/Irregular Capillary Ectasia: Dilated capillaries with diameters between 30–50 μm; parallel loops defined regular ectasia, while non-parallel loops indicated irregular ectasia.
- Filiform Elongated Capillaries: Presence of more than two thread-like elongated capillaries.
- Prominent Subpapillary Plexus: Apparent subpapillary plexus creating a network connecting capillaries.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as numbers and percentages (%). The normality of continuous data was assessed using the Kolmogorov–Smirnov test. Comparisons between groups were performed using Student's t-test for normally distributed variables and Mann–Whitney U test for non-normally distributed variables. Comparisons of continuous variables among three or more groups were performed using one-way ANOVA, and categorical variables were compared using the Chi-square or Fisher's Exact test. For subgroup comparisons with small sample sizes, exact methods such as the exact Mann–Whitney U test or Fisher's Exact Test were applied. These tests, while appropriate for small sample scenarios, may yield p-values of 1.000 even when minor numerical differences exist. Correlations between variables were assessed using Pearson correlation analysis. Receiver Operating Characteristic (ROC) curve analyses were performed within the RA patient group to evaluate the ability of arterial stiffness parameters (PWV, AIx75, reflection magnitude, peripheral resistance, and pulse pressure) to identify patients with elevated vascular stiffness. Cut-off points were determined based on the distribution of values within the RA cohort, and the clinical relevance was interpreted in the context of subclinical cardiovascular risk. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for significant cut-off values. Statistical analyses were performed using IBM SPSS version 26.0 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 was considered statistically significant.

RESULTS

The comparison of demographic and clinical parameters between patient and control groups is presented in Table 1. Mean age and BMI in the patient group were 45.53±8.68 years and 26.56±3.52 kg/m², respectively, whereas control group values were 45.15±9.12 years and 26.69±4.18 kg/m², respectively, without significant differences (p=0.776, p=0.826, respectively). Gender distribution also did not differ significantly between groups (p=0.073).

PWV, AIx75, reflection magnitude, and peripheral resistance were significantly higher in patients compared to controls (p<0.001, p=0.048, p=0.014, and p=0.011, respectively). Pulse pressure and pulse rates were similar between groups (p=0.091 and p=0.898, respectively).

Rates of regular capillary ectasia, tortuous capillaries, prominent subpapillary plexus, filiform elongated capillaries, and neoangiogenesis positivity were significantly higher in the patient group (p=0.001, p<0.001, p=0.004, p<0.001, and p=0.001, respectively). However, positivity rates for irregular capillary ectasia, microhemorrhage, and meandering (crossed) capillaries were similar between groups (p=0.126, p=0.363, and p=0.052, respectively) (Table 1).

The comparison of laboratory parameters between patient and control groups is shown in Table 2. ESR, anti-CCP, RF, CRP, and troponin levels were significantly higher in the patient group compared to the control group (p<0.001 for all). Conversely, albumin/globulin ratio was significantly higher in the control group (p<0.001). Positivity rates for anti-CCP, RF, and seropositivity in the patient group were 63.3%, 74.4%, and 80.0%, respectively, whereas these rates were 0.0%, 3.3%, and 3.3% in the control group (p<0.001 for each) (Table 2.).

The comparison of arterial stiffness parameters and troponin levels according to irregular capillary ectasia positivity in the patient group is presented in Table 3. Patients with irregular capillary ectasia positivity had significantly higher reflection magnitude values (62.39±7.41) compared to those without ectasia (58.72±8.47; p=0.034). However, no significant differences were observed in PWV, AIx75, peripheral resistance, pulse pressure, and troponin values between groups (p>0.05 for all) (Table 3).

Comparison of arterial stiffness parameters and troponin levels according to microhemorrhage positivity in the patient group is shown in Table 4. Patients with positive microhemorrhage had significantly higher PWV [8.7 (6.4-9.7) m/s] and pulse pressure values [56 (31-63) mmHg] compared to those without microhemorrhage [PWV: 6.9 (5-11.7); pulse pressure: 42 (18-73)] (p=0.048 and p=0.004, respectively). AIx75, reflection magnitude, peripheral resistance, and troponin values did not differ significantly between groups (p>0.05) (Table 4).

The comparison of arterial stiffness parameters and troponin levels according to meandering (crossed) capillary positivity in the patient group is shown in Table 5. AIx75 values were significantly higher in patients with meandering capillary positivity (30.42±8.09) compared to patients without

it (25.51±9.84; p=0.011). No significant differences were observed for PWV, reflection magnitude, peripheral resistance, pulse pressure, and troponin levels between groups (p>0.05 for all) (Table 5).

The comparison of arterial stiffness parameters, troponin levels, and capillaroscopic findings according to seropositivity in the patient group is presented in Table 6. Positivity rates of regular capillary ectasia, tortuous capillaries, prominent subpapillary plexus, filiform elongated capillaries, neoangiogenesis, capillary loss, microhemorrhage, and meandering capillaries did not differ significantly by seropositivity (p>0.05 for all). Seropositive patients showed significantly higher peripheral resistance (1714.99±150.82 vs. 1578.64±200.83; p=0.002) and lower pulse pressure values (41.69±10.63 vs. 48.61±10.02; p=0.014). However, PWV, AIx75, reflection magnitude, and troponin levels were not significantly different between seropositive and seronegative patients (p>0.05) (Table 6.).

In the patient group, arterial stiffness parameters and blood values were compared according to capillaroscopy findings. Patients with positive normal capillary patterns showed no significant differences in PWV, AIx75, reflection magnitude, peripheral resistance, pulse pressure, or troponin levels (p>0.05). Patients with positive regular capillary ectasia had significantly lower reflection magnitude values (58.44±8.64) compared to those without ectasia (62.10±7.40; p=0.034), while other parameters showed no significant differences (p>0.05). Positivity for tortuous capillaries, capillary loss, prominent subpapillary plexus, filiform elongated capillaries, and neoangiogenesis was not associated with significant differences in arterial stiffness or troponin levels (p>0.05). Biological agent use did not significantly affect capillaroscopic findings or arterial stiffness parameters (p>0.05). Regarding disease duration, positivity for filiform elongated capillaries was significantly higher in patients with disease duration of 2–5 years (48.1%) and >5 years (46.5%) compared to those with ≤1 year (15.8%; p=0.047). No significant associations were found between other capillaroscopic findings or arterial stiffness parameters and disease duration (p>0.05).

In the patient group, correlations between PWV, AIx75, reflection magnitude, peripheral resistance, pulse pressure, ESR, and CRP were evaluated. ESR levels showed a moderate positive correlation with CRP and AIx75 values (r=0.428, p<0.001; r=0.341, p=0.001, respectively). Additionally, a weak but significant positive correlation was observed between CRP and AIx75 (r=0.246, p=0.020).

The ROC analysis conducted in the RA group to evaluate the diagnostic utility of arterial stiffness markers in identifying patients with high vascular stiffness is presented in Table 7. These assessments are clinically relevant as they may help differentiate RA patients at higher cardiovascular risk, even in the absence of overt clinical disease. The cut-off value for PWV was ≥6.35 m/s (sensitivity: 72.2%, specificity: 62.2%, AUC±SE=0.755±0.036, p<0.001), AIx75 was ≥25.5% (sensitivity: 65.6%, specificity: 46.7%, AUC±SE=0.582±0.042, p=0.057), reflection magnitude was ≥61.15% (sensitivity: 48.9%, specificity: 66.7%, AUC±SE=0.601±0.042, p=0.019), peripheral resistance was ≥1612.65 dyn•s/cm (sensitivity: 74.4%, specificity: 43.3%, AUC±SE=0.587±0.043, p=0.044), and pulse pressure was ≥39.5 mmHg (sensitivity: 64.4%, specificity: 52.2%, AUC±SE=0.575±0.043, p=0.082) (Table 7, Figure 1).

Representative capillaroscopic images of tortuous capillaries, filiform elongation, and neoangiogenesis are shown in Figure 2.

Table 1. Comparison of Demographic and Clinical Parameters Between Patient and Control Groups

Parameter	Patient (n=90)	Control (n=90)	P-value
Age (years) (Mean±SD)	45.53±8.68	45.15±9.12	0.776
Body Mass Index (kg/m²)	26.56±3.52	26.69±4.18	0.826
Gender, n (%)			0.073
- Female	75 (83.3%)	65 (72.2%)	
- Male	15 (16.7%)	25 (27.8%)	
Disease duration (years)	5 (1-18)	-	-
Biological agent use (%)	30.0%	-	-
Circulatory Parameters			
PWV (m/s)	7.39±1.56	6.07±0.89	<0.001
AIx75 (%)	28.18±9.21	25.40±9.55	0.048
Reflection magnitude (%)	60.35±8.18	57.56±9.92	0.014
Peripheral resistance (dyn·s/cm)	1687.72±169.88	1619.96±184.14	0.011
Pulse pressure (mmHg)	43.07±10.81	40.56±8.90	0.091
Pulse (bpm)	82.18±13.00	81.94±12.57	0.898
Capillaroscopy Findings, n (%)			
Normal pattern	1 (1.1%)	10 (11.1%)	0.009
Giant capillaries	0 (0.0%)	0 (0.0%)	-
Regular capillary ectasia	43 (47.8%)	22 (24.4%)	0.001
Irregular capillary ectasia	40 (44.4%)	30 (33.3%)	0.126
Tortuous capillaries	70 (78.7%)	44 (48.9%)	<0.001
Capillary loss	5 (5.6%)	5 (5.6%)	1.000
Microhemorrhage	9 (10.0%)	13 (14.4%)	0.363
Prominent subpapillary plexus	33 (36.7%)	16 (17.8%)	0.004
Filiform elongated capillaries	36 (40.0%)	14 (15.6%)	<0.001
Neoangiogenesis	51 (56.7%)	28 (31.1%)	0.001
Meandering (crossed) capillaries	49 (54.4%)	36 (40.0%)	0.052
AIx75: Augmentation index; PWV: Pulse wave velocity.			

Table 2. Comparison of Laboratory Parameters Between Patient and Control Groups			
Parameter	Patient (n=90)	Control (n=90)	P-value
ESR [median (min-max)] (mm/h)	23 (2-82)	14 (1-52)	<0.001
Anti-CCP [median (min-max)]	51.5 (0.3-300)	0 (0-8)	<0.001
RF [median (min-max)] (IU/ml)	28.5 (0.6-702)	4.85 (0.8-36.9)	<0.001
CRP [median (min-max)] (mg/L)	5 (0.8-52)	2 (1-61)	<0.001
Albumin/Globulin	1.25±0.22	1.38±0.22	<0.001
Troponin [median (min-max)] (ng/L)	2.75 (0-28)	1.8 (0.5-8)	<0.001
Anti-CCP positivity (n,%)	57 (63.3%)	0 (0.0%)	<0.001
Rheumatoid factor positivity (n,%)	67 (74.4%)	3 (3.3%)	<0.001
Seropositivity (n,%)	72 (80.0%)	3 (3.3%)	<0.001
CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; RF: Rheumatoid factor; Anti-CCP: Anti-cyclic citrullinated peptide.			

Table 3. Comparison of Arterial Stiffness Parameters and Troponin Levels According to Irregular Capillary Ectasia Positivity in the Patient Group			
Parameter	**Irregular capillary ectasia positive (n=40)**	**Irregular capillary ectasia negative (n=50)**	**P-value**
PWV (m/s)	7.36±1.53	7.42±1.60	0.875
AIx75 (%)	27.42±9.80	28.08±8.76	0.485
Reflection magnitude (%)	62.39±7.41	58.72±8.47	0.034
Peripheral resistance (dyn·s/cm)	1692.09±174.13	1684.23±168.90	0.829
Pulse pressure (mmHg)	44.02±10.53	42.32±11.09	0.461
Troponin (ng/L)	2.94±2.01	3.92±4.00	0.161
AIx75: Augmentation index; PWV: Pulse wave velocity			

Table 4. Comparison of Arterial Stiffness Parameters and Troponin Levels According to Microhemorrhage Positivity in the Patient Group			
Parameter	**Microhemorrhage positive (n=9) [median (min-max)]**	**Microhemorrhage negative (n=81) [median (min-max)]**	**P-value**
PWV (m/s)	8.7 (6.4-9.7)	6.9 (5-11.7)	0.048
AIx75 (%)	31 (12-36)	28 (8-47)	1.000
Reflection magnitude (%)	61.0 (48.8-75.0)	61.1 (39.5-75.6)	0.968
Peripheral resistance (dyn·s/cm)	1711.3 (1376.3-1922.6)	1696.9 (1200-2166.3)	0.614
Pulse pressure (mmHg)	56 (31-63)	42 (18-73)	0.004
Troponin (ng/L)	2.8 (1.5-6.3)	2.7 (0-28)	0.467
Alx75: Augmentation index, PWV: Pulse wawe velocity,P-values were calculated using exact Mann–Whitney U test for continuous variables and Fisher's Exact Test for categorical variables due to small subgroup sizes			

Table 5. Comparison of Arterial Stiffness Parameters and Troponin Levels According to Meandering (Crossed) Capillary Positivity in the Patient Group			
Parameter	**Meandering capillary positive (n=49) (Mean±SD)**	**Meandering capillary negative (n=41) (Mean±SD)**	**P-value**
PWV (m/s)	7.54±1.51	7.22±1.62	0.342
AIx75 (%)	30.42±8.09	25.51±9.84	0.011
Reflection magnitude (%)	61.07±8.41	59.50±7.91	0.368
Peripheral resistance (dyn·s/cm)	1697.94±160.78	1675.51±181.41	0.536
Pulse pressure (mmHg)	44.97±10.27	40.80±11.14	0.068
Troponin (ng/L)	3.69±4.00	3.24±2.18	0.568
AIx75: Augmentation index; PWV: Pulse wave velocity			

Table 6. Comparison of Capillaroscopy Findings and Arterial Stiffness Parameters According to Seropositivity in the Patient Group			
Parameter	**Seropositive (n=72)**	**Seronegative (n=18)**	**P-value**
Capillaroscopy Findings (n,%)			
Normal pattern	1 (1.4%)	0 (0.0%)	1.000
Giant capillaries	0 (0.0%)	0 (0.0%)	-
Regular capillary ectasia	31 (43.1%)	12 (66.7%)	0.073
Irregular capillary ectasia	30 (41.7%)	10 (55.5%)	0.304
Tortuous capillaries	54 (75.6%)	16 (88.9%)	0.340
Capillary loss	4 (5.6%)	1 (5.6%)	1.000
Microhemorrhage	7 (9.7%)	2 (11.1%)	1.000
Prominent subpapillary plexus	29 (40.3%)	4 (22.2%)	0.182
Filiform elongated capillaries	29 (40.3%)	7 (38.9%)	0.914
Neoangiogenesis	44 (61.1%)	7 (38.9%)	0.113
Meandering (crossed) capillaries	36 (50.0%)	13 (72.2%)	0.116
Arterial Stiffness (Mean±SD)			
PWV (m/s)	7.49±1.60	7.02±1.37	0.259
AIx75 (%)	27.68±9.22	30.22±9.14	0.298
Reflection magnitude (%)	59.97±8.12	61.87±8.10	0.383
Peripheral resistance (dyn·s/cm)	1714.99±150.82	1578.64±200.83	0.002
Pulse pressure (mmHg)	41.69±10.63	48.61±10.02	0.014
Troponin (ng/L)	3.64±3.58	3.88±1.59	0.385
AIx75: Augmentation index; PWV: Pulse wave velocity			

Table 7. Cut-Off Values and ROC Analysis Results for PWV, AIx75, Reflection Magnitude, Peripheral Resistance, and Pulse Pressure								
Parameter	**Cut-off**	**Sensitivity (%)**	**Specificity (%)**	**PPV**	**NPV**	**AUC**	**95% CI**	**P-value**
PWV (m/s)	≥6.35	72.2	62.2	65.7	69.1	0.755	0.685-0.824	<0.001
AIx75 (%)	≥25.5	65.6	46.7	55.1	57.5	0.582	0.499-0.665	0.057
Reflection magnitude (%)	≥61.15	48.9	66.7	59.5	56.6	0.601	0.518-0.685	0.019
Peripheral resistance (dyn·s/cm)	≥1612.65	74.4	56.8	56.3	62.9	0.587	0.517-0.683	0.040
Pulse pressure (mmHg)	≥39.5	64.4	52.2	57.3	59.6	0.607	0.524-0.689	0.014
AIx75: Augmentation index; AUC: Area under the curve; NPV: Negative predictive value; PPV: Positive predictive value; PWV: Pulse wave velocity.								

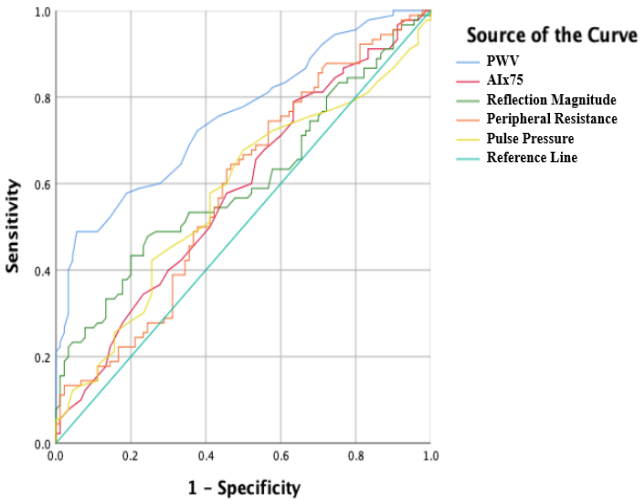

Figure 1. ROC curves for PWV, AIx75, reflection magnitude, peripheral resistance, and pulse pressure

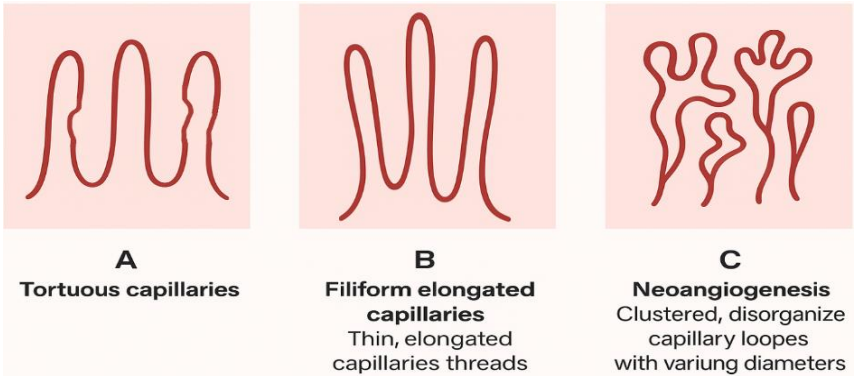

Figure 2. Representative nailfold videocapillaroscopy (NVC) images of key findings observed in RA patients.
(A) Tortuous capillaries: Note the irregular looping morphology and increased tortuosity.
(B) Filiform elongated capillaries: Thin, elongated capillary loops resembling threads.
(C) Neoangiogenesis: Clustered, disorganized capillary loops with varying diameters and disrupted architecture.

DISCUSSION

The present study demonstrated that patients with RA exhibit significantly higher arterial stiffness and more frequent capillaroscopic abnormalities compared to healthy controls, consistent with the known vascular implications of chronic systemic inflammation. These findings are in line with previous studies indicating that RA is associated with subclinical atherosclerosis and microvascular dysfunction. PWV and AIx75, as non-invasive markers of arterial stiffness, have been validated as surrogate indicators of cardiovascular risk; however, their sensitivity to hemodynamic fluctuations and inter-individual variability should be acknowledged as limitations. Similarly, while NVC offers valuable insight into microvascular architecture, its diagnostic reliability can be affected by factors such as temperature, observer variability, and the lack of standardized classification in RA. Therefore, while the associations observed in our study are noteworthy, they should be interpreted with caution, particularly in the absence of longitudinal outcome data.

Our results, showing elevated PWV and AIx75 values in RA patients, support their established role as sensitive indicators of arterial stiffness and reinforce previous findings regarding the vascular consequences of chronic systemic inflammation in RA. Abdulmajid et al., in a recent meta-analysis, similarly confirmed increased arterial stiffness parameters, notably PWV, in RA patients compared to controls, reflecting a higher cardiovascular risk profile.(15) Additionally, Ambrosino et al. demonstrated that every 10 mmHg increase in pulse pressure was associated with a 13–20% increase in cardiovascular mortality.(16) However, in our study, although pulse pressure was elevated in RA patients, it did not reach statistical significance compared to controls, possibly due to the applied exclusion criteria (absence of hypertension and hyperlipidemia).

Capillaroscopic findings in our RA patients, including regular capillary ectasia, tortuous capillaries, prominent subpapillary plexus, filiform elongated capillaries, and neoangiogenesis, were significantly more common compared to the control group. Similar observations were reported by Redisch et al., who found significant increases in tortuous capillaries, filiform elongated capillaries, and prominent subpapillary plexus in RA patients.(17) Consistent with our results, Said et al. also reported significantly increased tortuous and ectatic capillaries in RA patients compared to healthy controls.(18) Moreover, a larger study by Dima et al. involving 430 RA patients demonstrated higher neoangiogenesis and tortuous capillaries in RA patients.(19) These findings underline the importance of nailfold capillaroscopy as an early diagnostic tool in detecting microvascular changes associated with systemic inflammatory processes in RA.

In our study, microhemorrhage positivity significantly correlated with higher PWV and pulse pressure, which are established markers of arterial stiffness and predictors of cardiovascular risk. A meta-analysis by Blacher et al. emphasized that each 10-mmHg increment in pulse pressure significantly increased cardiovascular mortality by 13%–20%.(20) Our findings are consistent with Forsberg et al., who highlighted microhemorrhages as markers of endothelial damage and microvascular dysfunction, potentially contributing to increased arterial stiffness.(21)

We found significant differences regarding arterial stiffness parameters based on capillaroscopic findings. Patients with irregular capillary ectasia had significantly higher reflection magnitude values, indicating an association between microvascular abnormalities and arterial stiffness. This aligns partially with findings reported by Redisch et al., who showed a pronounced increase in capillary abnormalities, including elongated and tortuous capillaries, which might be associated with early vascular damage in RA.(17)

Interestingly, seropositive patients in our study exhibited significantly higher peripheral resistance but lower pulse pressure, without significant differences in PWV or AIx75 compared to seronegative patients. Kim et al., in contrast, reported a significant association between seropositivity and higher PWV values, suggesting a link between seropositivity and arterial stiffness, potentially attributable to inflammation severity differences.(22) The discrepancy between our findings and those by Kim et al. might be related to differences in study population characteristics, disease severity, or sample sizes.

Our study extends current literature by simultaneously evaluating arterial stiffness parameters and capillaroscopic findings in RA patients and healthy controls. While prior studies separately assessed arterial stiffness or capillaroscopic findings in RA, our investigation uniquely integrates these assessments to explore potential associations between macrovascular and microvascular changes. Previous research, including meta-analyses by Popescu et al. and Blacher et al., primarily focused on arterial stiffness markers or cardiovascular risk independently, without detailed correlations to microvascular abnormalities.(2, 20) Conversely, studies such as those by Rajaei et al. and Kim et al. primarily explored capillaroscopic abnormalities in RA patients without evaluating arterial stiffness simultaneously.(22, 23) Our combined methodological approach provides comprehensive insights into both vascular domains, highlighting significant associations and interactions that were previously underreported in the literature.

Our study has some limitations. First, the relatively small sample size may limit the generalizability of our findings to the broader RA population. Second, due to the cross-sectional nature of the study, causal relationships between arterial stiffness and capillaroscopic findings could not be firmly established. Moreover, this design precludes the assessment of predictive utility regarding cardiovascular events. The lack of longitudinal follow-up and outcome data limits our ability to determine whether the observed vascular changes are truly indicative of future cardiovascular risk. Additionally, we did not evaluate longitudinal changes in arterial stiffness and capillaroscopic parameters, which might have provided insight into their progression and prognostic value. Some subgroup analyses were based on small sample sizes, which may have reduced the statistical power and increased the risk of Type II error, potentially masking true associations. Finally, despite rigorous exclusion criteria, the influence of undetected confounding factors cannot be entirely ruled out and may have affected the accuracy of our results. Nevertheless, this study is, to our knowledge, the first to concurrently evaluate arterial stiffness parameters and detailed capillaroscopic findings in RA patients, providing valuable initial insights and forming a foundation for future longitudinal and multicenter studies.

Notably, we observed a higher-than-expected prevalence of certain capillaroscopic abnormalities—particularly tortuous and meandering capillaries—even in the healthy control group. This finding appears inconsistent with some previously published data reporting lower frequencies in non-rheumatic populations. Several plausible factors may account for this discrepancy. While all control participants were free of diagnosed systemic rheumatologic disease, subclinical or functional vascular alterations could still be present due to environmental and behavioral influences. Variables such as frequent exposure to cold, occupational hand use, emotional stress, and caffeine intake are known to transiently alter capillary morphology. Moreover, the southeastern region of Türkiye, where the study was conducted, presents distinct climatic and lifestyle characteristics that may predispose individuals to non-specific capillary changes. These considerations underscore the importance of cautious interpretation of capillaroscopic abnormalities in non-rheumatic individuals, emphasizing the need for context-specific reference standards in future research.

Although our findings demonstrate a significant association between arterial stiffness and capillaroscopic abnormalities in RA patients, the potential implications for cardiovascular risk prediction must be interpreted with caution. These results may reflect underlying subclinical vascular dysfunction associated with systemic inflammation. However, in the absence of validated cardiovascular risk stratification tools (e.g., SCORE, Framingham risk score) or surrogate imaging markers of atherosclerosis (such as carotid intima-media thickness or coronary artery calcium scoring), definitive conclusions regarding prognostic utility cannot be made. Therefore, we propose that the observed associations highlight a promising direction for future investigation rather than establishing predictive value. Prospective, longitudinal studies incorporating clinical outcomes and cardiovascular risk stratification are warranted to further elucidate the clinical utility of these vascular markers in RA populations.

CONCLUSION

This study demonstrates that rheumatoid arthritis patients exhibit significantly increased arterial stiffness parameters and characteristic capillaroscopic abnormalities compared to healthy controls. Our findings indicate a notable association between microvascular changes and arterial stiffness in RA patients, suggesting that combined evaluation of capillaroscopy and arterial stiffness parameters may help detect subclinical vascular alterations. However, further longitudinal studies are needed to assess their predictive value for cardiovascular outcomes. Further longitudinal studies are warranted to clarify the predictive value of these parameters for cardiovascular outcomes and to validate their integration into clinical practice for comprehensive cardiovascular risk assessment in RA patients.

Ethics Committee Approval: Ethical approval was obtained from the Gaziantep University Faculty of Medicine non-invasive clinical research ethics committee (Approval number: 2022/452, Date: 01.02.2023).

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