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BIOCHEMICAL AND ULTRASOUND MARKERS OF EARLY CARDIOVASCULAR DAMAGE IN PATIENTS WITH SPONDYLOARTHRITIS

ABSTRACT

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The dissertation consists of 141 standard pages and is illustrated with 30 tables and 33 figures. The bibliography includes 363 references**,** of which 1 in Cyrillic and 362 in Latin script. The dissertation was reviewed and approved for public defense at a meeting of the Departmental Council of the Department of Propedeutics of Internal Medicine, Medical University “Prof. Dr. Paraskev Stoyanov” – Varna**.**

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LIST OF ABBREVIATIONS

AS – Ankylosing Spondylitis

BMI – Body Mass Index

IMD – Inflammatory Joint Disease (ВСЗ – Възпалително ставно заболяване)

IBD-SpA – Inflammatory Bowel Disease-associated Spondyloarthritis (ВЧЗ-СпА)

DAS28 – Disease Activity Score-28

ESR – Erythrocyte Sedimentation Rate

LDL – Low-Density Lipoprotein

NSAIDs – Nonsteroidal Anti-Inflammatory Drugs

PsA – Psoriatic Arthritis

SpA – Spondyloarthritis

uSpA – Undifferentiated Spondyloarthritis (нСпА)

CRP – C-Reactive Protein

MRI – Magnetic Resonance Imaging

CHOL – Cholesterol

ACo – Arterial Compliance

AIP – Atherogenic Index of Plasma

AI – Augmentation Index

ASAS – Assessment of SpondyloArthritis International Society

ASDAS – Ankylosing Spondylitis Disease Activity Score

BASDAI – Bath Ankylosing Spondylitis Disease Activity Index

BASFI – Bath Ankylosing Spondylitis Functional Index

CASPAR – Classification Criteria for Psoriatic Arthritis

CIMT – Carotid Intima-Media Thickness

CREC – Cross-Reactive Epitope Cluster

ELISA – Enzyme-Linked Immunosorbent Assay

EP – Elastic Modulus

ESSG – European Spondyloarthropathy Study Group

EULAR – European Alliance of Associations for Rheumatology

FMD – Flow-Mediated Dilatation

HDL – High-Density Lipoprotein

HLA-B27 – Human Leukocyte Antigen B27

HT-hypertension

ICAM-1 – Intercellular Adhesion Molecule-1

IDL – Intermediate-Density Lipoprotein

IFN-γ – Interferon gamma

IL-6, IL-17, IL-23 – Interleukins 6, 17, 23

ILC – Innate Lymphoid Cells

IMT – Intima-Media Thickness

JAK – Janus Kinase

MHC – Major Histocompatibility Complex

MMP – Matrix Metalloproteinases

NK – Natural Killer cells

NO – Nitric Oxide

NOD – Nucleotide-binding Oligomerization Domain

PASI – Psoriasis Area and Severity Index

PECAM – Platelet Endothelial Cell Adhesion Molecule

PWV – Pulse Wave Velocity

RA – Rheumatoid Arthritis

RANKL – Receptor Activator of Nuclear Factor Kappa-B Ligand

SCORE / SCORE2 – Systematic Coronary Risk Evaluation

STAT3 – Signal Transducer and Activator of Transcription 3

TNF-α – Tumor Necrosis Factor alpha

VCAM-1 – Vascular Cell Adhesion Molecule-1

VEGF – Vascular Endothelial Growth Factor

I. INTRODUCTION

Spondyloarthritides (SpA) represent a heterogeneous group of inflammatory rheumatic diseases sharing common clinical and etiological features. They are characterized by involvement of the axial and/or peripheral skeleton, enthesitis, extra-articular manifestations, and a strong association with the human leukocyte antigen HLA-B27. This group includes ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), enteropathic arthritis (IBD-SpA), juvenile spondyloarthritis, and undifferentiated spondyloarthritis (uSpA). In an effort to unify the different forms of the disease and facilitate early diagnosis, the ASAS international society proposed a new classification, dividing SpA into axial and peripheral forms according to the predominant clinical involvement. The prototype of the axial form is AS, while PsA serves as the prototype of the peripheral form, with both conditions being the most common in clinical practice.

In recent years, growing evidence has demonstrated increased morbidity and mortality from cardiovascular diseases among patients with AS and PsA. This population is known to exhibit alterations in lipid profile, insulin resistance, and other metabolic risk factors. Furthermore, accumulating data point to structural and functional vascular changes, supporting the hypothesis of accelerated atherosclerosis in SpA. Inflammation plays a central role in this pathogenic link, not only influencing traditional risk factors but also directly contributing to endothelial injury and the development of atherosclerotic changes.

Within this context, the need for reliable non-invasive methods for early detection of subclinical atherosclerosis in SpA patients is of particular importance. Among the most promising approaches is the use of single-point echo-tracking technology, which enables the assessment of local arterial stiffness (AS) in the common carotid artery. This parameter has been shown to strongly correlate with aortic stiffness and to have prognostic value regarding the development of atherosclerosis. Although reference values for local arterial stiffness have been established in healthy individuals, such data

are currently lacking for patients with inflammatory joint diseases, which complicates the interpretation of results in clinical practice.

In parallel with imaging diagnostics, serum biomarkers are attracting increasing scientific interest as tools to help identify patients at elevated vascular risk. Particular attention has been directed to adhesion molecules such as VCAM-1 and ICAM-1, whose expression is elevated in atherosclerotic plaques and associated with the vulnerability of atheromatous lesions. Data from prospective studies have demonstrated the prognostic value of elevated serum levels of soluble forms of these molecules in both asymptomatic individuals and patients at high cardiovascular risk. They are considered potential markers not only for subclinical atherosclerosis but also for the assessment of future cardiovascular events.

Increased expression of adhesion molecules has also been documented in other pathological conditions, including inflammatory, autoimmune, neoplastic, and psychiatric diseases. The link between chronic inflammation and atherosclerosis is well established, and in patients with inflammatory joint diseases this association remains an active area of research. Despite advances, further studies are needed to validate adhesion molecules as biomarkers for the early diagnosis of subclinical atherosclerosis in patients with ankylosing spondylitis and psoriatic arthritis. The present study aims to evaluate vascular ultrasonographic parameters and adhesion molecule levels as potential markers of subclinical atherosclerosis in this patient population.

II. Aim and Objectives of the Study

The primary aim of the present study is to evaluate the role of vascular ultrasonographic parameters and adhesion molecules as markers of early atherosclerosis in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). The study seeks to determine whether the inflammatory process underlies the development of vascular changes and whether specific differences exist between the two disease entities and compared to healthy controls. Additionally, it analyzes the

interactions between inflammatory activity, lipid metabolism, and arterial stiffness in the context of cardiovascular risk.

To achieve this aim, the study sets out the following specific objectives:

1. To compare vascular ultrasound parameters (CIMT, β-stiffness, PWV, AI, ACo, EP) between patients with ankylosing spondylitis, psoriatic arthritis, and healthy controls in order to assess arterial stiffness between the groups.
2. To analyze and compare the levels of adhesion molecules VCAM-1 and ICAM-1 among the three study groups, considering their role as markers of endothelial dysfunction.
3. To evaluate the relationship between disease activity (ASDAS-CRP, BASDAI, DAS28), inflammatory markers (CRP, ESR), and vascular parameters within each group, and to identify potential differences between them.
4. To compare the lipid profile, atherogenic indices, and cardiovascular risk scores between patients with ankylosing spondylitis, psoriatic arthritis, and controls, and to examine their associations with vascular changes and adhesion molecules.
5. To assess the influence of demographic and clinical factors (sex, age, arterial hypertension, smoking status, therapeutic status) on vascular, laboratory, and clinical parameters in patients with spondyloarthritis.

III. Materials and Methods

1. Research Setting

The study was conducted at the following departments of the University Hospital "St. Marina" – Varna and the Medical University – Varna:

- Department of Internal Medicine, University Hospital "St. Marina" – Varna
- Department of Rheumatology, University Hospital "St. Marina" – Varna

- Department of Clinical Immunology, University Hospital “St. Marina” – Varna
- Department of Clinical Laboratory, University Hospital “St. Marina” – Varna

2. Study Population

A total of **154 participants** were included in the study, divided into three groups:

- **83 patients with ankylosing spondylitis (AS)**, diagnosed according to the Assessment of SpondyloArthritis International Society (ASAS) criteria for axial spondyloarthritis.
- **40 patients with psoriatic arthritis (PsA)**, fulfilling the CASPAR (ClASsification criteria for Psoriatic ARthritis) classification criteria.
- **31 individuals in a control group**, without evidence of inflammatory joint disease or established cardiovascular pathology.

All participants were selected based on preliminary screening carried out at the Department of Internal Medicine and the Department of Rheumatology, University Hospital “St. Marina” – Varna, during the period **2023–2024**. Patients were followed up on an outpatient basis or hospitalized under clinical procedure №42, with the diagnostic process and therapeutic approach adhering to established standards and the recommendations of EULAR.

The control group consisted of volunteers with similar demographic characteristics (sex, age, and body mass index), without a history of autoimmune, endocrine, metabolic, cardiovascular, or neoplastic disease.

Prior to enrollment, all participants signed an **informed consent form**. Ethical approval for the study was obtained from the **Ethics Committee of the Medical University – Varna**, in accordance with applicable regulatory and ethical requirements for research involving human subjects.

3.1. Inclusion Criteria

Participants were eligible for the study if they met the following conditions:

- **Ankylosing spondylitis (AS) group:**
  - Age over 18 years;
  - Diagnosis of ankylosing spondylitis according to the ASAS (Assessment of SpondyloArthritis International Society) classification criteria for axial spondyloarthritis;
  - Signed informed consent for participation.
- **Psoriatic arthritis (PsA) group:**
  - Age over 18 years;
  - Diagnosis of psoriatic arthritis according to the CASPAR (ClASsification criteria for Psoriatic ARthritis) criteria;
  - Current or past history of psoriasis;
  - Signed informed consent for participation.
- **Control group:**
  - No evidence of inflammatory joint disease;
  - No active cardiovascular, autoimmune, metabolic, chronic infectious, or neoplastic pathology;
  - Age- and sex-matched to the study groups;
  - Signed informed consent for participation.

3.2. Exclusion Criteria

Participants were excluded from the study if they had any of the following conditions:

- Documented ischemic heart disease, cerebrovascular disease, or peripheral arterial disease;
- Heart failure, arrhythmias, conduction disorders, or cardiomyopathies;
- Type 1 or type 2 diabetes mellitus, or metabolic syndrome;
- Chronic kidney disease (CKD ≥ stage 3 according to KDIGO);
- Chronic obstructive pulmonary disease (COPD);

- Active infection, neoplastic disease, or immunodeficiency;
- Pregnancy or breastfeeding;
- Inability to undergo ultrasonographic examination due to technical reasons.

4. Documentation and Data Sources

Information about study participants was collected through direct clinical examination, structured interview, and review of available medical records. For patients with ankylosing spondylitis and psoriatic arthritis, data were obtained from outpatient visits, hospital discharge summaries, laboratory test results, and imaging studies documented in their medical files. For the control group, data were collected through direct medical history taking, physical examination, and investigations performed according to a standardized protocol.

For each participant, an **individual registration form** was completed, including: demographic data, clinical diagnosis (for patients), disease duration, ongoing pharmacological therapy, smoking status, blood pressure measurements, laboratory and ultrasonographic parameters, as well as results of disease activity assessments. All documentation was stored under conditions ensuring confidentiality and protection of personal data, in accordance with the regulations of the Medical University – Varna and national ethical standards.

Data collection and interpretation were carried out by a **multidisciplinary team** consisting of a rheumatologist, an internist, a cardiologist, and a clinical immunologist. All specialists had expertise in their respective fields and were affiliated with the University Hospital “St. Marina” – Varna. The study protocol was pre-developed and approved by the Ethics Committee of the Medical University – Varna.

All participants provided **written informed consent** prior to inclusion, in accordance with the **Declaration of Helsinki**. The study was approved by the University Ethics Committee for Scientific Research, Protocol №133/22.06.2023.

5. Instrumental Examinations

All study participants underwent ultrasonographic assessment of the right common carotid artery using an **Aloka Hitachi Prosound α7** ultrasound system equipped with a high-frequency linear transducer. The examination was performed with the participant in the supine position, the neck extended, and the head slightly rotated at an angle of approximately 30° contralateral to the side under investigation. Measurements were obtained 2 cm proximal to the carotid bifurcation, in a longitudinal section, allowing for optimal visualization and a perpendicular ultrasound beam relative to the vessel wall.

In addition, **carotid intima-media thickness (CIMT)**—a well-established morphological marker of early subclinical atherosclerosis—was measured in all participants. CIMT was recorded at the most clearly visualized segment of the posterior wall of the right common carotid artery, in an area free of atherosclerotic plaques or calcifications. Three measurements were obtained during different cardiac cycles, and the mean value was calculated.

After vessel visualization, the **echo-tracking function** was activated, enabling automated monitoring of changes in arterial diameter. Using visual markers, vessel boundaries were defined at the level of the tunica media–adventitia interface of both the near and far walls. The examination was synchronized with an **electrocardiographic (ECG) recording** via peripheral electrodes, which allowed for precise identification of the onset of systolic and diastolic phases of the cardiac cycle. To improve diagnostic accuracy, participants were instructed to hold their breath during the registration of at least six consecutive cardiac cycles.

The generated curves reflected the dynamic changes in arterial diameter, from which the built-in software algorithm automatically calculated the following indices of arterial stiffness:

- **β-stiffness index**
- **Pulse wave velocity β (PWVβ)**

- **Arterial compliance (ACo)**
- **Augmentation index (AIx)**
- **Pressure-strain elastic modulus (Ep)**

For precise computation, values of systolic and diastolic blood pressure, measured in advance, were entered into the system, allowing for a comprehensive and objective assessment of arterial elasticity using a validated mathematical model.

6. Laboratory Investigations

6.1 Lipoproteins, CRP, ESR

All laboratory tests were performed in the certified units of the Clinical Laboratory at University Hospital *"St. Marina"* – Varna. Venous blood samples were collected in the morning after an overnight fast, followed by centrifugation and processing according to standard pre-analytical requirements. The biochemical and inflammatory parameters included:

- **C-reactive protein (CRP):** measured by an immunoturbidimetric method on the automated biochemical analyzer ADVIA 1800 + IMMULITE 2000i;
- **Erythrocyte sedimentation rate (ESR):** determined by the Westergren method using the automated analyzer Sysmex 1000XN;
- **Total cholesterol (CHOL), high-density lipoproteins (HDL-C), low-density lipoproteins (LDL-C), and triglycerides (TG):** measured using the ADVIA 1800 biochemical analyzer.

6.2 Investigation of Adhesion Molecules

The measurement of adhesion molecules was conducted in the Department of Immunology at University Hospital *"St. Marina"* – Varna.

6.2.1 Determination of Serum Levels of sVCAM-1

Serum levels of sVCAM-1 were determined using the commercial **Human sVCAM-1 ELISA Kit** (catalog no. Invitrogen BMS232, Thermo Fisher Scientific,

USA), with a sensitivity (detection limit) of 0.6 ng/ml and a linear range of 3.15–100 ng/ml.

The tested material was venous blood serum collected in a closed system with serum separation gel (Vacutainer SST II Advance, Becton Dickinson). After venipuncture, blood was left at room temperature for 30 minutes to allow clotting, followed by centrifugation at 1,000 × g for 15 minutes. Serum samples were stored at –80 °C until analysis.

The sVCAM-1 assay was performed according to the manufacturer's protocol as follows:

1. Each well of the plate was washed twice with 300 µl of Wash Buffer.
2. 100 µl of working Assay Buffer was added to all wells.
3. 100 µl of diluted standards and blank (Assay Buffer) were added to the designated wells.
4. 100 µl of diluted unknown and control samples (dilution 1:50; 10 µl sample + 490 µl Assay Buffer) were added to the remaining wells within 15 minutes.
5. 50 µl of the conjugate solution (biotin-conjugated anti-human VCAM-1 antibody and streptavidin-conjugated horseradish peroxidase) was added to each well.
6. The plate was sealed with adhesive film and incubated for 2 hours at room temperature on a microplate shaker.
7. The contents of the wells were aspirated and washed three times with 300 µl Wash Buffer. After the final wash, wells were thoroughly emptied and blotted on absorbent paper.
8. 100 µl of TMB substrate solution was added to each well and incubated for 10 minutes at room temperature.
9. 100 µl of Stop Solution was added to each well.
10. Optical density was measured within 30 minutes at 450 nm with a correction at 630 nm using a Microplate Reader MIT511-4 (Nicesound Electronics Group).

11. The concentration of sVCAM-1 (ng/ml) was calculated based on the corresponding standards using a four-parameter logistic nonlinear regression model (MikroWin 2000, version 4.31, Mikrotek Laborsysteme GmbH). The final concentrations of unknown and control samples were multiplied by the dilution factor (50).

6.2.2 Determination of Serum Levels of sICAM-1

Serum levels of sICAM-1 were determined using the commercial **Human sICAM-1 ELISA Kit** (catalog no. Invitrogen BMS201, Thermo Fisher Scientific, USA), with a sensitivity (detection limit) of 2.2 ng/ml and a linear range of 6.25–100 ng/ml.

The tested material was venous blood serum collected in a closed system with serum separation gel (Vacutainer SST II Advance, Becton Dickinson). After venipuncture, blood was left at room temperature for 30 minutes to allow clotting, followed by centrifugation at 1,000 × g for 15 minutes. Serum samples were stored at –80 °C until analysis.

The sICAM-1 assay was performed according to the manufacturer's protocol as follows:

1. Each well of the plate was washed twice with 300 µl Wash Buffer.
2. 100 µl of diluted standards and blank (Sample Diluent) were added to the designated wells.
3. To the remaining wells, 90 µl of Sample Diluent and 10 µl of unknown and control samples (dilution 1:10) were added within 15 minutes.
4. 50 µl of HRP-conjugated antibody was added to each well.
5. The plate was sealed with adhesive film and incubated for 1 hour at room temperature on a microplate shaker.
6. The contents of the wells were aspirated and washed three times with 300 µl Wash Buffer. After the final wash, wells were thoroughly emptied and blotted on absorbent paper.

7. 100 µl of TMB substrate solution was added to each well and incubated for 10 minutes at room temperature.
8. 100 µl of Stop Solution was added to each well.
9. Optical density was measured within 30 minutes at 450 nm with a correction at 630 nm using a Microplate Reader MIT511-4 (Nicesound Electronics Group).
10. The concentration of sICAM-1 (ng/ml) was calculated based on the corresponding standards using a four-parameter logistic nonlinear regression model (MikroWin 2000, version 4.31, Mikrotek Laborsysteme GmbH). The final concentrations of unknown and control samples were multiplied by the dilution factor (10).

7. Calculated Indices

In addition to the directly measured laboratory and ultrasonographic parameters, a number of secondary indices were calculated for all participants to assess atherogenic risk, hemodynamic profile, and overall cardiovascular risk.

Body height (cm) and weight (kg) were measured, and **body mass index (BMI)** was calculated using the formula:

BMI=weight (kg)/height (m)2

7.1. Atherogenic Indices

To evaluate lipid-mediated atherogenic risk, the following parameters were calculated:

- **Castelli Risk Index I (CRI-I)** = Total cholesterol / HDL-cholesterol
- **Castelli Risk Index II (CRI-II)** = LDL-cholesterol / HDL-cholesterol
- **Atherogenic Index of Plasma (AIP)** = log (Triglycerides / HDL-cholesterol)
- **Atherogenic Coefficient (AtC)** = (Total cholesterol – HDL-cholesterol) / HDL-cholesterol
- **Non-HDL cholesterol (non-HDL)** = Total cholesterol – HDL-cholesterol

7.2. Hemodynamic Indices

For assessment of blood pressure and arterial stiffness, the following parameters were calculated:

- **Pulse pressure (PP)** (mmHg) = Systolic arterial pressure (SBP) – Diastolic arterial pressure (DBP)
- **Mean arterial pressure (MAP)** (mmHg) = DBP + (SBP – DBP)/3

7.3. Cardiovascular Risk Scores

Each participant was assessed using three validated tools for estimating the individual 10-year cardiovascular risk:

- **Framingham Risk Score** – based on age, sex, systolic blood pressure, lipid fractions, smoking status, and presence of diabetes mellitus.
- **SCORE2** – European model for assessing overall (fatal + non-fatal) 10-year risk of a first cardiovascular event (myocardial infarction or stroke), based on age, sex, smoking status, total cholesterol, and systolic blood pressure. Calibration for Bulgaria was applied.
- For participants aged ≥70 years, cardiovascular risk was assessed using **SCORE2-OP**.

Risk values were interpreted according to established reference thresholds for low, moderate, high, and very high risk, in line with the current **ESC** and **NICE** guidelines.

8. Assessment of Inflammatory Activity

Inflammatory activity in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA) was assessed using validated composite indices specific to each disease.

For patients with AS, the **ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score – C-reactive protein)** was applied. This index combines patient-reported outcomes (back pain, duration of morning stiffness, global assessment of disease activity, and peripheral pain/swelling) with an objective inflammatory

marker—C-reactive protein (CRP, mg/L). The score was calculated according to the official formula of the Assessment of SpondyloArthritis International Society (ASAS):

ASDAS-CRP = 0.121 × back pain + 0.058 × duration of morning stiffness + 0.110 × patient's global assessment + 0.073 × peripheral pain/swelling + 0.579 × ln(CRP + 1)

According to published reference thresholds, disease activity was classified into the following categories:

- <1.3 – inactive disease
- 1.3–2.1 – low activity
- 2.1–3.5 – high activity
- 3.5 – very high activity

For patients with PsA, inflammatory activity was assessed using the **DAS28 (Disease Activity Score using 28 joint counts)**. This index includes the number of tender and swollen joints (from 28 joints), the patient's global health assessment on a visual analogue scale (VAS, 0–100 mm), and CRP levels (mg/L). The score was calculated using a validated online DAS28-CRP calculator, based on the following formula:

DAS28-CRP = 0.56 × √(TJC28) + 0.28 × √(SJC28) + 0.36 × ln(CRP + 1) + 0.014 × GH + 0.96

Where:

- **TJC28** – number of tender joints (out of 28)
- **SJC28** – number of swollen joints (out of 28)
- **CRP** – C-reactive protein (mg/L)
- **GH** – global health assessment by the patient (0–100 mm on VAS)

Interpretation of DAS28 values:

- <2.6 – remission
- 2.6–3.2 – low disease activity
- 3.2–5.1 – moderate disease activity

- 5.1 – high disease activity

9. Statistical Methods

Data processing and statistical analysis were performed using **IBM SPSS Statistics, version 27.0**. All data were entered into an electronic database and verified for errors and missing values.

- **Categorical variables** were presented as absolute numbers and percentages.
- **Continuous variables** were expressed as mean ± standard deviation (SD) for normally distributed data or as median (interquartile range, IQR) for non-normally distributed data.

Normality of distribution was tested using the **Shapiro–Wilk** and **Kolmogorov–Smirnov** tests. In cases of deviation from normality ($p < 0.05$), non-parametric methods were applied.

- For comparison between three independent groups (AS, PsA, and controls), the **Kruskal–Wallis test** was used.
- For comparison between two groups, the **Mann–Whitney U test** was applied.
- **Categorical variables** were compared using **Pearson's chi-square test**.

Correlation between continuous quantitative variables was assessed using **Spearman's correlation analysis**, with calculation of correlation coefficients (rho) and p-values for statistical significance.

To investigate the independent effects of clinical, biochemical, and anthropometric variables on vascular ultrasound indices and cardiovascular risk scores, **multiple linear regression analysis** (Enter method) was performed. The following dependent variables were used: carotid intima-media thickness (CIMT), β-stiffness index, pulse wave velocity (PWV), arterial compliance (ACo), elastic modulus (EP), vascular adhesion molecule VCAM-1, and SCORE. Independent variables (predictors) included age, sex, smoking status, presence of arterial hypertension, BMI, CRP, LDL, triglycerides, AIP, and VCAM-1, depending on the specific aim of the analysis.

Model adequacy was evaluated using the coefficient of determination (R^2), F-test values, residual analysis, and the **Durbin–Watson statistic**. Models were considered statistically significant at **$p < 0.05$**.

The results were presented in tables and figures, including **box plots**, **correlation diagrams**, and **diagnostic scatter plots** for regression models.

10. General Clinical and Demographic Characteristics

As an initial characterization of the study population, basic demographic indicators, including age, were analyzed. The mean age of participants with ankylosing spondylitis (AS) was **47.05 ± 10.62 years**, among patients with psoriatic arthritis (PsA) – **54.03 ± 11.01 years**, and in the control group – **48.35 ± 11.27 years**. A trend was observed for PsA patients to be older compared with the other groups, consistent with the later clinical manifestation of the disease.

Detailed information on the main clinical and demographic characteristics of the participants is summarized in **Table 7**, while the distribution of age by groups is visualized in **Figure 1 (Box plot)**.

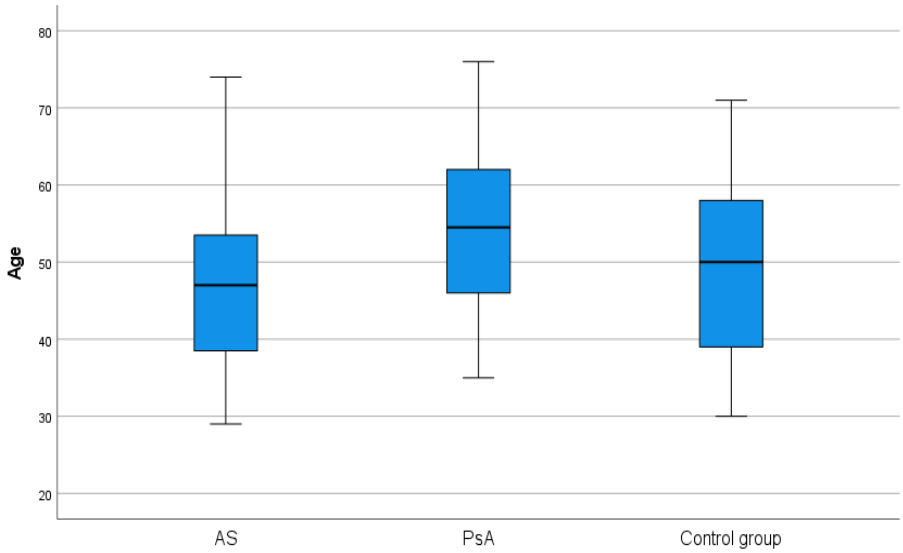

Figure 1. Distribution of age by groups

Table 7. Main clinical and demographic characteristics of the participants by groups

Indicator	AS (n = 83)	PsA (n = 40)	Controls (n = 31)
Mean age (years)	47.05 ± 10.62	54.03 ± 11.01	48.35 ± 11.27
Sex (% male)	66.3%	32.5%	54.8%
Sex (% female)	33.7%	67.5%	45.2%
Mean BMI (kg/m²)	27.75 ± 5.31	28.47 ± 5.64	26.73 ± 4.78
Smoking (% smokers)	55.4%	65.0%	64.5%
Arterial hypertension (%)	27.7%	47.5%	35.5%

To evaluate the potential influence of age on biochemical, vascular, and cardiovascular parameters, participants were stratified into three age subgroups:

- **Young** (≤45 years),
- **Middle-aged** (46–60 years),
- **Older** (>60 years).

The distribution of participants by age categories is shown in **Figure 2**, with a predominance of individuals in the young and middle-aged groups.

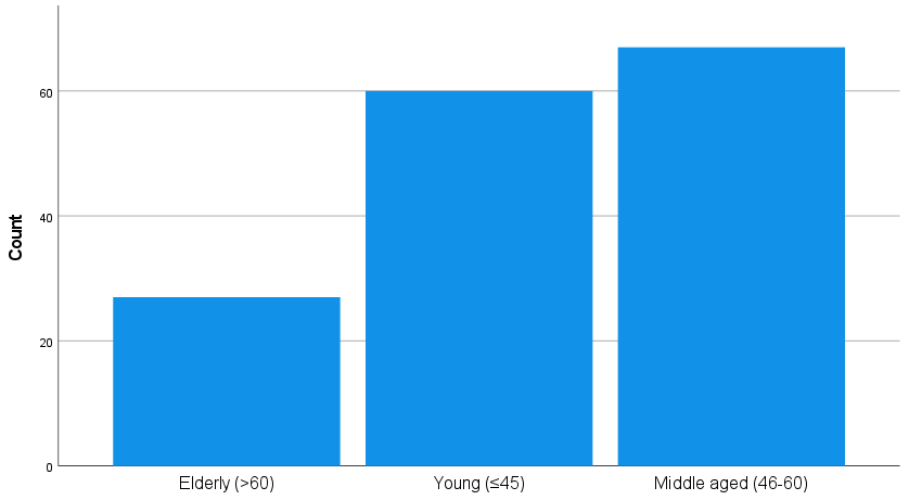

Figure 2. Distribution by age categories

When analyzing the subgroups by age, no statistically significant differences were observed in most of the investigated parameters, including inflammatory markers (ESR, CRP), lipid profile (Total cholesterol, LDL, HDL, TG), vascular ultrasound indices (CIMT, PWV, β-stiffness, AI, ACo, EP), cardiovascular risk scores (Framingham, SCORE2), atherogenic indices, and adhesion molecules (ICAM, VCAM).

In addition, disease duration was assessed among the included patients. In individuals with ankylosing spondylitis, disease duration ranged from **0.8 to 30 years**, with a mean of **9.49 ± 6.04 years**. In the psoriatic arthritis group, duration varied between **1 and 37 years**, with a mean of **9.43 ± 7.70 years**. The similarity between the two groups in this parameter reflects a comparable clinical disease duration in the studied population.

With regard to sex distribution, men predominated in the ankylosing spondylitis group (**66.3%**), whereas in psoriatic arthritis the opposite trend was observed, with a predominance of women (**67.5%**). The control group showed a relatively balanced sex distribution (**54.8% men vs. 45.2% women**).

Alongside disease duration, other key clinical parameters were analyzed. The **body mass index (BMI)** was highest among patients with psoriatic arthritis (**28.47 ± 5.64 kg/m²**), followed by those with ankylosing spondylitis (**27.75 ± 5.31 kg/m²**) and the control group (**26.73 ± 4.78 kg/m²**). A wide range of BMI values was observed across all three groups, spanning from underweight to marked obesity.

With respect to smoking status, the proportion of smokers was **65.0%** among PsA patients, **55.4%** in AS patients, and **64.5%** in the control group. The distribution of smokers and non-smokers across the groups is illustrated in **Figure 3**.

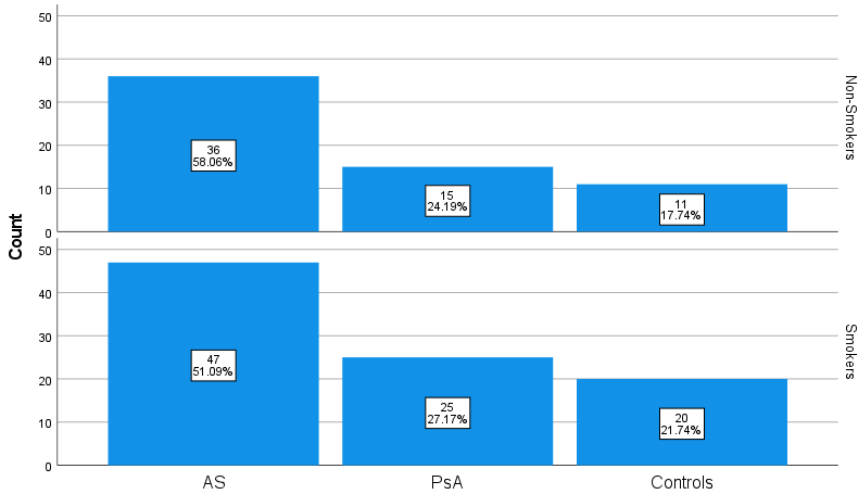

Figure 3. Proportion of smokers and non-smokers by study groups

Analysis of blood pressure demonstrated that the mean systolic pressure for the entire sample was **123.67 ± 9.86 mmHg** (min. 104, max. 165 mmHg), while the mean diastolic pressure was **77.27 ± 6.30 mmHg** (min. 60, max. 95 mmHg). The mean arterial pressure was **92.73 ± 6.59 mmHg**, and the mean pulse pressure was **46.40 ± 8.34 mmHg**.

Arterial hypertension was identified in **47.5%** of patients with psoriatic arthritis, **27.7%** of those with ankylosing spondylitis, and **35.5%** of participants in the control group (**Figure 4**).

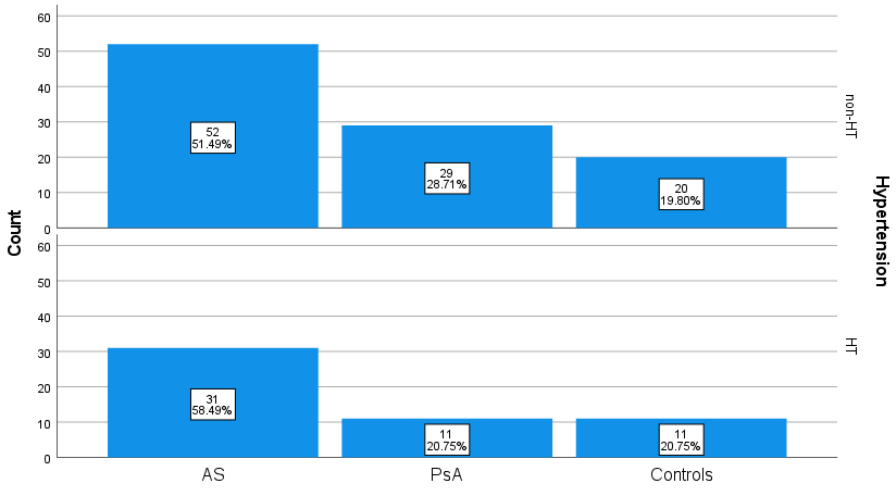

Figure 4. Percentage distribution of participants with and without arterial hypertension across groups (AS, PsA, and controls).

HT – hypertensive disease; Non- HT – no hypertensive disease.

In the overall study population (**n = 123**), the distribution of patients by type of targeted therapy is presented in **Figure 5**. The largest proportion of participants were treated with **anti-TNF agents (n = 58)**, followed by **anti-IL-17 therapies (n = 32)** and **JAK inhibitors (n = 13)**. A total of **20 patients** were biologic-naïve, having not received any targeted therapy at the time of inclusion.

Among patients with ankylosing spondylitis, the most frequently used therapy was **anti-TNF (60.2%)**, followed by **anti-IL-17 (14.5%)** and **JAK inhibitors (7.2%)**, while **18.1%** of participants were biologic-naïve (**Figure 6**).

In the psoriatic arthritis group, the largest proportion of patients received **anti-IL-17 therapy (50.0%)**, while **20.0%** were treated with **anti-TNF agents**, **17.5%** with **JAK inhibitors**, and **12.5%** were biologic-naïve (**Figure 7**).

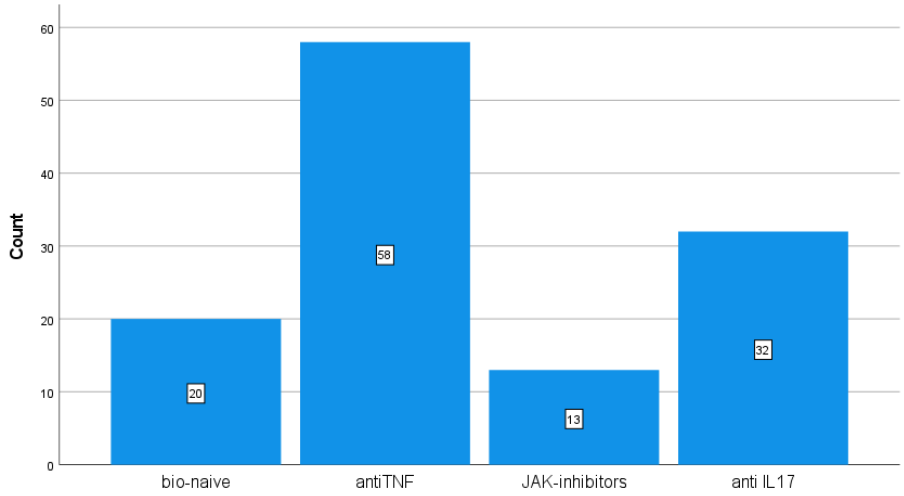

Figure 5. Distribution of targeted therapies in the overall patient sample.

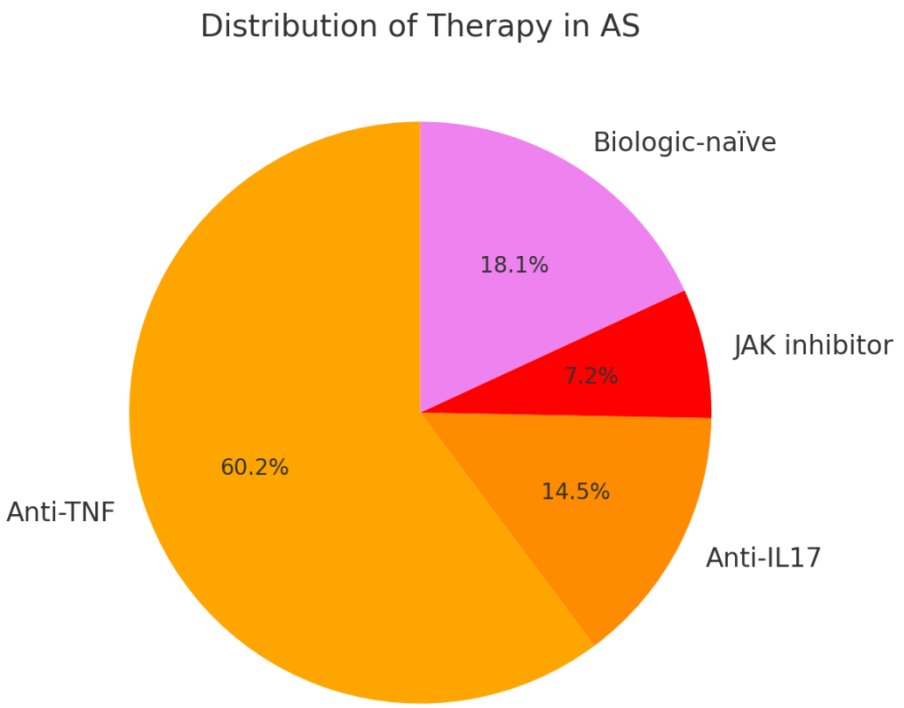

Figure 6. Distribution of therapies in patients with ankylosing spondylitis.

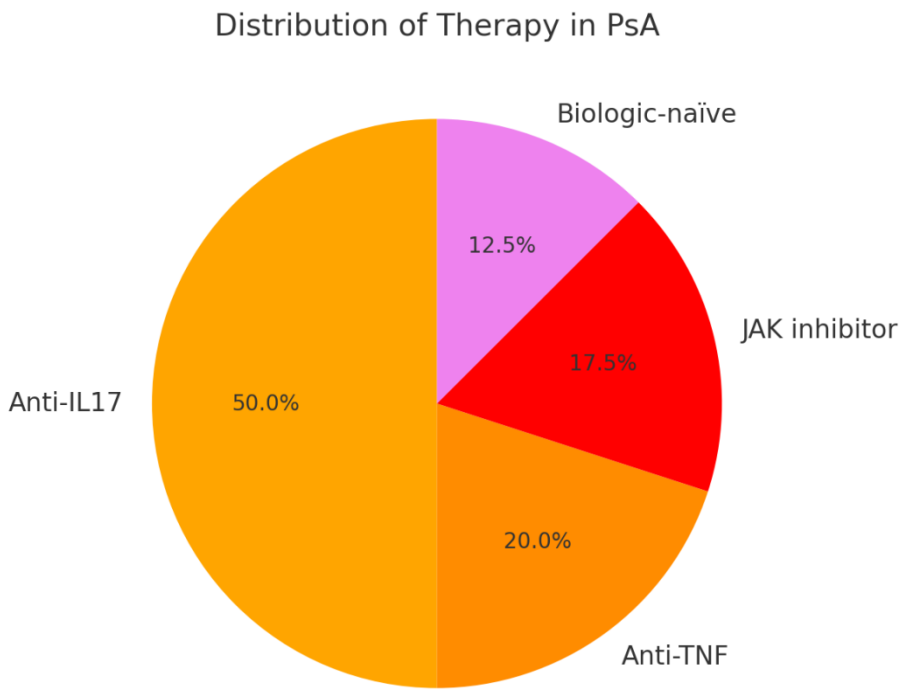

Figure 7. Distribution of therapies in patients with psoriatic arthritis.

11. Disease Activity and Inflammatory Markers

Statistically significant differences in inflammatory markers were observed among the three groups. Patients with ankylosing spondylitis (AS) demonstrated the highest median values of **ESR (22 mm/h)** and **CRP (6.3 mg/L)**, followed by the psoriatic arthritis (PsA) group (**ESR: 16 mm/h; CRP: 4.1 mg/L**). The control participants showed values within the normal range (**ESR: 9 mm/h; CRP: 1.8 mg/L**).

Regarding disease activity, in the AS group the mean **ASDAS-CRP** was **2.30 ± 1.30** (range: 1.13–6.90), reflecting the presence of patients across the full spectrum from low to high activity. The mean **BASDAI** was **2.83 ± 1.96**, corresponding to low to moderate activity.

Among PsA patients, the **DAS28** ranged from **2.06 to 5.89**, with a mean of **2.82 ± 0.83**, indicating that the majority of participants had low to moderate disease activity.

12. Lipid Profile and Atherogenic Indices

Analysis of the lipid profile revealed similar mean total cholesterol values across the three groups: **5.38 ± 1.21 mmol/L** in AS, **5.44 ± 1.17 mmol/L** in PsA, and **5.16 ± 0.86 mmol/L** in controls.

Mean triglyceride levels were highest among controls (**1.58 ± 0.97 mmol/L**) and lowest among PsA patients (**1.43 ± 0.78 mmol/L**).

LDL cholesterol levels were comparable between AS (**3.25 ± 1.08 mmol/L**) and PsA (**3.29 ± 0.94 mmol/L**), while slightly lower in the control group (**2.93 ± 0.80 mmol/L**). HDL cholesterol was lowest in AS (**1.44 ± 0.41 mmol/L**), slightly higher in PsA (**1.49 ± 0.37 mmol/L**), and highest among controls (**1.54 ± 0.44 mmol/L**).

The mean non-HDL cholesterol—a marker of atherogenic lipid fraction—was similar across all groups: **3.95 ± 1.12 mmol/L** in AS, **3.93 ± 1.11 mmol/L** in PsA, and **3.62 ± 0.86 mmol/L** in controls.

Calculated atherogenic indices showed a tendency toward higher atherogenicity in patients with inflammatory diseases. The **atherogenic coefficient** was highest in AS (**2.97 ± 1.22**) and PsA (**2.97 ± 1.72**) compared with controls (**2.58 ± 1.05**). The **Atherogenic Index of Plasma (AIP, log TG/HDL-C)** was slightly negative in all groups (AS: **–0.61 ± 0.318**; PsA: **–0.45 ± 0.289**; Controls: **–0.52 ± 0.290**), consistent with a generally low to moderate cardiovascular risk profile.

Table 8. Lipid profile and atherogenic indices across the three study groups

Parameter	AS (n=83)	PsA (n=40)	Controls (n=31)
Total cholesterol (mmol/L)	5.38 ± 1.21	5.44 ± 1.17	5.16 ± 0.86
Triglycerides (mmol/L)	1.48 ± 1.46	1.43 ± 0.78	1.58 ± 0.97
LDL (mmol/L)	3.25 ± 1.08	3.29 ± 0.94	2.93 ± 0.80
HDL (mmol/L)	1.44 ± 0.41	1.49 ± 0.37	1.54 ± 0.44
Non-HDL (mmol/L)	3.95 ± 1.12	3.93 ± 1.11	3.62 ± 0.86
Atherogenic coefficient	2.97 ± 1.22	2.97 ± 1.72	2.58 ± 1.05
AIP (log TG/HDL-C)	–0.61 ± 0.318	–0.45 ± 0.289	–0.52 ± 0.290

Castelli Index I	3.95 ± 1.13	3.83 ± 1.13	3.58 ± 1.05
Castelli Index II	2.38 ± 0.88	2.33 ± 0.85	2.10 ± 0.95

13. Cardiovascular Risk Scores

Assessment of cardiovascular risk using the **Framingham** and **SCORE2** scales revealed differences among AS, PsA, and control groups.

According to the **Framingham score**, mean risk was **5.43 ± 4.91** in AS, **5.27 ± 4.34** in PsA, and **6.76 ± 4.48** in controls. Despite numerical differences, values were relatively close, suggesting no major increase in Framingham-defined risk among patients with inflammatory arthritis.

More distinct differences were observed with the **SCORE2** index. PsA patients exhibited the highest mean score (**11.52 ± 7.69**), followed by AS (**8.61 ± 6.72**), while the lowest values were recorded in controls (**8.89 ± 6.24**). This finding may reflect more pronounced metabolic disturbances or accumulation of risk factors among PsA patients.

14. Vascular Ultrasound Parameters

Significant differences in vascular ultrasound parameters were observed among the three groups. The mean **CIMT** value was highest in PsA patients (**0.6383 ± 0.2044 mm**), followed by AS patients (**0.5980 ± 0.2008 mm**) and controls (**0.5184 ± 0.0959 mm**), indicating more pronounced arterial changes in the inflammatory groups.

Pulse wave velocity (PWV) was also increased in PsA (**6.33 ± 1.30 m/s**) and AS (**5.99 ± 0.96 m/s**) compared with controls (**5.32 ± 0.63 m/s**). A similar trend was observed for the **β-stiffness index**, with the highest value in PsA (**8.85 ± 3.76**), followed by AS (**7.36 ± 2.40**) and controls (**5.76 ± 1.20**).

The **augmentation index (AI)** was elevated in PsA (**19.41 ± 13.56**) and AS (**16.70 ± 14.11**) compared with controls (**14.94 ± 18.74**), although the control group showed greater variability.

Arterial compliance (ACo) was lowest in PsA patients (**0.8053 ± 0.3150 mm²/kPa**), consistent with the values in AS (**1.0131 ± 1.1124**) and controls (**1.0171 ± 0.3808**). Similarly, the **elastic modulus (EP)** was highest in PsA (**113.6 ± 50.0 kPa**), followed by AS (**97.5 ± 32.2 kPa**) and controls (**77.5 ± 17.9 kPa**), further supporting the presence of increased arterial stiffness in patients with inflammatory arthropathies.

Table 9. Mean vascular ultrasound parameters in the three study groups

Group	CIMT (mm)	PWV (m/s)	β-stiffness	AI (%)	ACo (mm²/kPa)	Ep (kPa)
AS	0.5980 ± 0.2008	5.99 ± 0.96	7.36 ± 2.40	16.70 ± 14.11	1.0131 ± 1.1124	97.5 ± 32.2
PsA	0.6383 ± 0.2044	6.33 ± 1.30	8.85 ± 3.76	19.41 ± 13.56	0.8053 ± 0.3150	113.6 ± 50.0
Controls	0.5184 ± 0.0959	5.32 ± 0.63	5.76 ± 1.20	14.94 ± 18.74	1.0171 ± 0.3808	77.5 ± 17.9

15. Adhesion Molecules (ICAM, VCAM)

The mean values of ICAM and VCAM in AS, PsA, and control groups showed some differences. VCAM levels were higher in PsA patients (**927.15 ng/mL**) compared with AS (**813.94 ng/mL**) and controls (**852.10 ng/mL**). ICAM values were relatively similar between groups, with slightly higher mean values in the control group.

These results suggest a role for adhesion molecules in the pathogenesis of inflammatory arthropathies, with VCAM potentially having particular significance in PsA.

Table 10. Mean values of ICAM-1 and VCAM-1 in the three study groups

Group	ICAM (mean ± SD)	VCAM (mean ± SD)
AS	460.93 ± 145.52	813.94 ± 262.98
PsA	463.74 ± 127.97	927.15 ± 377.20
Controls	492.91 ± 130.15	852.10 ± 214.57

16. Subgroup Comparative Analysis

16.1 Comparison between AS, PsA, and Controls

16.1.1 Demographic Characteristics

Sex distribution differed clearly across groups: men predominated in AS (**66.3%**), whereas women were more common in PsA (**67.5%**). The control group showed a nearly balanced sex ratio (**54.8% men vs. 45.2% women**).

Mean age also varied significantly between groups (**Kruskal–Wallis H = 10.824, p = 0.004**), with AS patients being the youngest (**46.6 ± 9.8 years**), followed by PsA (**51.7 ± 11.4 years**) and controls (**54.2 ± 8.3 years**).

The prevalence of arterial hypertension tended to be higher in PsA (**47.5%**) than in AS (**27.7%**) and controls (**35.5%**), but did not reach statistical significance (χ^2 = **4.703, p = 0.095**).

Table 11. Demographic and clinical characteristics of the study groups

Indicator	AS (n=83)	PsA (n=40)	Controls (n=31)	p-value
Sex (male)	66.3%	32.5%	54.8%	0.002
Arterial hypertension	27.7%	47.5%	35.5%	0.095
Smokers	55.4%	65.0%	64.5%	0.497

BMI did not differ significantly between groups (**Kruskal–Wallis H = 0.925, p = 0.630**), with mean values within the overweight range. The highest BMI was observed in PsA patients (**28.7 kg/m²**) and the lowest in controls (**25.9 kg/m²**).

No statistically significant differences were detected between the groups regarding systolic (p = 0.900), diastolic (p = 0.367), pulse (p = 0.415), or mean arterial pressure (p = 0.889). This suggests that, despite the presence of inflammatory activity and associated metabolic disturbances in AS and PsA, blood pressure remained relatively homogeneous across groups and likely does not represent an independent

distinguishing factor for cardiovascular risk in this population. These findings should be interpreted cautiously, taking into account the potential effects of antihypertensive therapy, different prevalence of hypertension, and variation in age and BMI.

16.1.2 Inflammatory Markers

The Kruskal–Wallis test confirmed significant differences for ESR ($p = 0.012$) and CRP ($p = 0.016$) between groups (AS, PsA, controls). Peak CRP levels were found in AS patients, followed by PsA, with the lowest values in controls. A similar trend was observed for ESR, with patients with spondyloarthropathies showing clearly elevated values compared with the control group.

16.1.3 Lipid Profile and Atherogenic Indices

The mean ranks of lipid parameters and atherogenic indices across the three groups are presented in **Table 12**. Despite the observed variations, no statistically significant differences were found for any of the analyzed parameters.

The lowest mean ranks for LDL cholesterol, non-HDL cholesterol, and Castelli indices were recorded in the control group, consistent with expectations of a healthier lipid profile among non-diseased individuals. However, the differences between groups did not reach statistical significance (all $p > 0.05$). No significant differences were detected for total cholesterol, HDL, triglycerides, or the calculated indices (atherogenic coefficient, AIP, Castelli I/II).

Table 12. Comparison of lipid parameters between the three groups

Parameter	AS (n=83)	PsA (n=40)	Controls (n=31)	p-value
Total cholesterol	78.99	79.05	71.52	0.705
LDL cholesterol	80.52	80.26	65.85	0.266
HDL cholesterol	73.74	80.29	83.97	0.497
Triglycerides	73.23	80.05	85.65	0.382
Non-HDL cholesterol	80.81	77.94	68.06	0.397
Atherogenic coefficient	82.40	74.71	67.97	0.276
AIP index	75.99	78.58	80.16	0.892
Castelli Index I	78.23	83.78	67.45	0.303
Castelli Index II	78.73	84.31	65.40	0.194

Despite variations in mean ranks, no statistically significant differences were found between groups for any of the lipid fractions (total cholesterol, LDL, HDL, triglycerides, non-HDL) or calculated indices (atherogenic coefficient, AIP, Castelli I/II). The lowest mean ranks for LDL, non-HDL, and Castelli indices were observed in the control group, which corresponds to expectations, but differences did not reach statistical significance (all $p > 0.05$).

16.1.4 Comparison of Cardiovascular Risk Across Patient Groups

When comparing mean ranks for the **Framingham score**, the values were similar across the three groups: AS (**77.31**), PsA (**72.53**), and controls (**79.35**). The resulting p-value (**p = 0.648**) indicated no statistically significant difference between groups for this parameter, suggesting a comparable Framingham-defined risk in the studied populations (**Figure 8**).

Analysis of the **SCORE2 index** also did not reveal statistically significant differences between groups (**p = 0.146**). The lowest mean rank was observed in the control group (**44.06**), followed by AS patients (**58.23**), with the highest values recorded in PsA (**72.65**). Although statistical significance was not reached, a trend toward higher SCORE2 values in PsA patients was noted, which may reflect a greater accumulation of cardiovascular risk factors in this group (**Figure 9**).

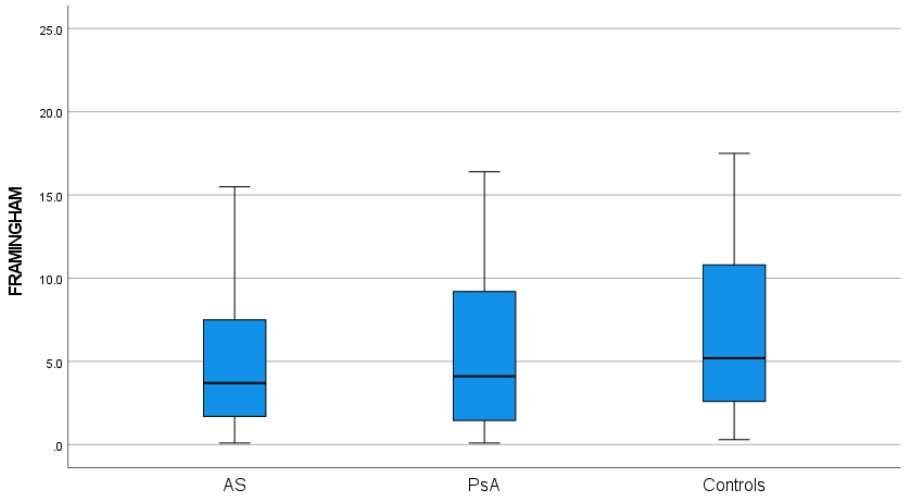

Figure 8. Cardiovascular risk profile according to the Framingham score across groups

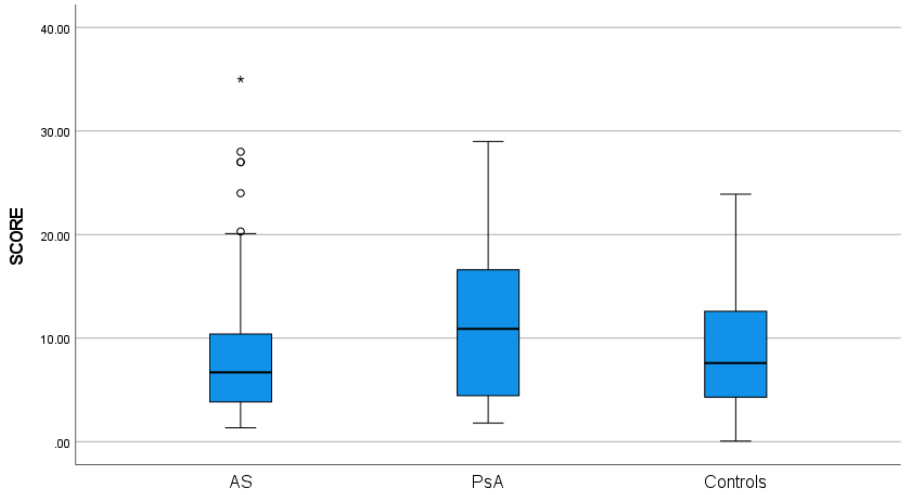

Figure 9. Cardiovascular risk profile according to the SCORE2 index across groups

16.1.4 Comparison of Vascular Ultrasound Parameters Across Groups

Analysis of vascular ultrasound parameters among the three groups—patients with ankylosing spondylitis (AS), psoriatic arthritis (PsA), and healthy controls—using the **Kruskal–Wallis test** revealed statistically significant differences for the following indices: **carotid intima–media thickness (CIMT)** (p = 0.013; *Figure 10*), **β-stiffness index** (p < 0.001; *Figure 11*), **pulse wave velocity (PWV)** (p = 0.001; *Figure 12*), **arterial compliance (ACo)** (p = 0.032; *Figure 13*), and **elastic modulus (Ep)** (p = 0.001; *Figure 14*).

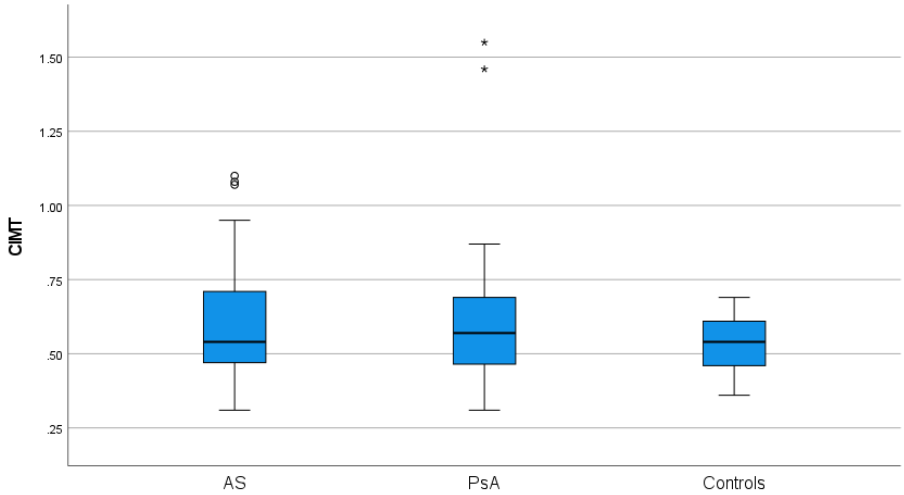

Figure 10. Comparison of carotid intima–media thickness (CIMT) across groups (AS, PsA, controls)

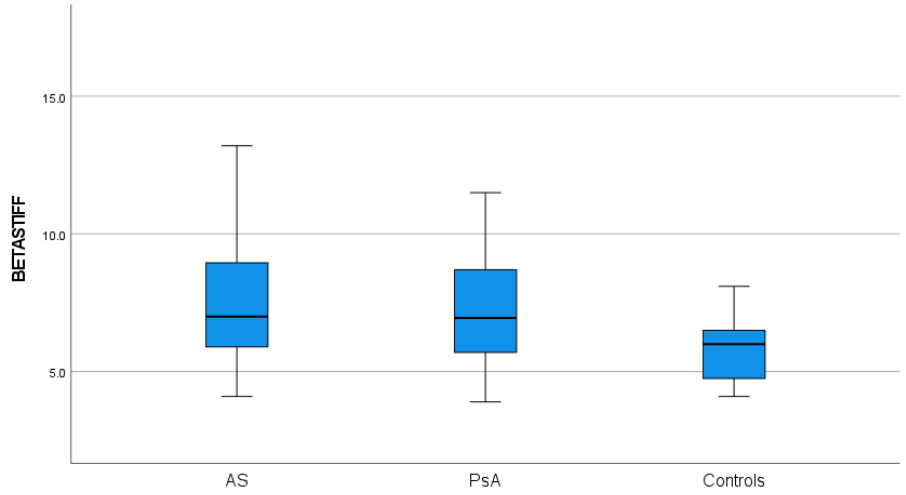

Figure 11. Distribution of β-stiffness index in the three study groups (AS, PsA, controls)

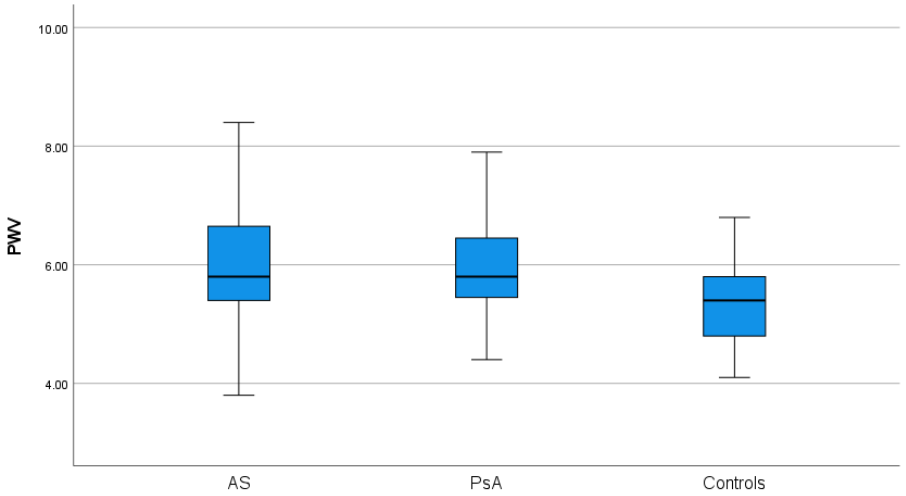

Figure 12. Comparison of pulse wave velocity (PWV) across groups (AS, PsA, controls)

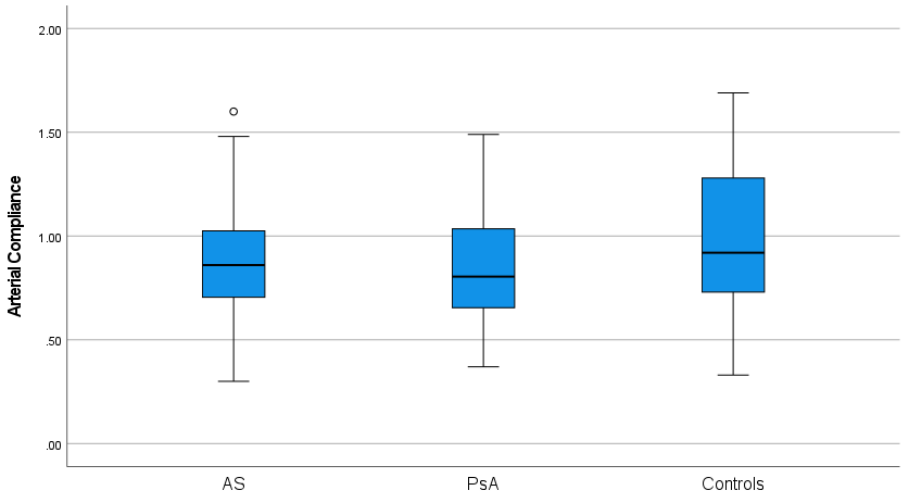

Figure 13. Comparison of arterial compliance (ACo) across groups (AS, PsA, controls)

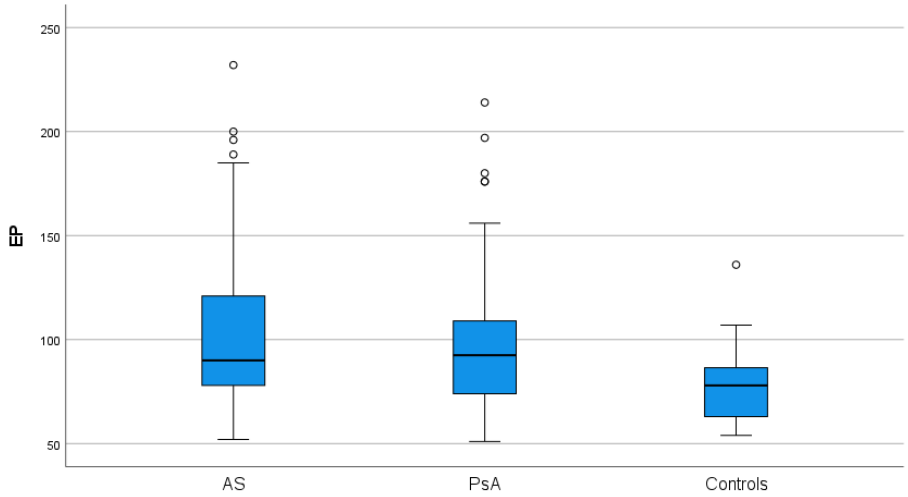

Figure 14. Distribution of elastic modulus (Ep) across groups (AS, PsA, controls)

Subsequent pairwise comparisons using the **Mann–Whitney U test** showed that, when comparing AS and controls, the parameters CIMT, β-stiffness, PWV, and Ep were higher in AS patients. Statistically significant differences were observed for **β-stiffness ($p < 0.001$)**, **PWV ($p < 0.001$)**, and **Ep ($p = 0.001$)**, while CIMT demonstrated borderline significance (**$p = 0.062$**). The difference in ACo did not reach significance (**$p = 0.181$**).

When comparing PsA patients and controls, all five indices demonstrated statistically significant differences in favor of the PsA group: **CIMT ($p = 0.002$)**, **β-stiffness ($p < 0.001$)**, **PWV ($p = 0.001$)**, **ACo ($p = 0.015$)**, and **Ep ($p = 0.002$)**.

Comparison between AS and PsA groups revealed no statistically significant differences, despite a trend toward higher values in PsA.

Table 13. Comparison of vascular ultrasound parameters across groups

Vascular parameter	AS vs Controls (p)	PsA vs Controls (p)	AS vs PsA (p)
CIMT	0.062	0.002	0.152
β-stiffness	<0.001	<0.001	0.105
PWV	<0.001	0.001	0.399
ACo	0.181	0.015	0.062
Ep	<0.001	0.002	0.349

16.1.5 Comparison of Adhesion Molecules (ICAM and VCAM) Across Groups

Comparison of **intercellular adhesion molecule (ICAM-1)** and **vascular cell adhesion molecule-1 (VCAM-1)** levels among the three study groups—AS, PsA, and healthy controls—did not reveal statistically significant differences.

For ICAM, the mean ranks were **73.23** (AS), **84.83** (PsA), and **79.48** (controls). Despite a trend toward higher values in PsA, the **Kruskal–Wallis test** did not reach significance (**H = 1.902, p = 0.386**). A similar pattern was observed for VCAM-1, where the mean ranks were **71.36 (AS)**, **89.89 (PsA)**, and **77.97 (controls)**, again without statistical significance (**H = 4.665, p = 0.097**). These results suggest that circulating levels of ICAM and VCAM did not differ substantially between groups in this cohort.

16.2 Comparison by Age Subgroups

When comparing the three age categories—**<45 years**, **45–60 years**, and **>60 years**—statistically significant differences were found only for **pulse pressure (p = 0.030)**, **SCORE2**, and **Framingham scores**, with higher values observed in older participants. This aligns with the expected age-related decline in arterial elasticity.

For other indices, such as the **elastic modulus (Ep)**, borderline significance was observed (**p = 0.059**), suggesting potential clinical relevance despite not reaching the conventional threshold for statistical significance.

16.3 Comparison by Sex

Analysis of biochemical and vascular ultrasound parameters by sex revealed several statistically significant differences.

- **Age:** Women in the cohort were significantly older than men (Mean Rank = **86.96 vs. 69.82**; **p = 0.024**, Mann–Whitney U test) (*Figure 15*).
- **CIMT:** Women demonstrated higher CIMT compared with men (Mean Rank = **86.96 vs. 69.82**; **p = 0.017**) (*Figure 16*). Although male sex is typically associated with higher cardiovascular risk and CIMT, the present

findings may reflect the influence of age distribution and other risk factors, warranting further stratification.

- **Augmentation Index (AI):** Women exhibited significantly higher AI values compared with men (**p < 0.001**), consistent with literature linking elevated AI to shorter body height and sex-related differences in arterial compliance (*Figure 17*).
- **SCORE2:** Men had a significantly higher SCORE2 cardiovascular risk (**p = 0.033**), which is expected given that sex is included as a risk factor in the SCORE2 algorithm.
- **Castelli Indices:** Both Castelli I and Castelli II indices were significantly higher in men compared with women (**p = 0.003 and p = 0.019**, respectively) (*Figures 18 and 19*), reflecting well-documented sex-specific differences in lipid profile and cardiovascular risk.

No statistically significant differences between sexes were observed for inflammatory markers (ESR, CRP), lipid fractions (total cholesterol, TG, LDL, HDL), or vascular indices such as β-stiffness, PWV, ACo, and Ep (all p > 0.05).

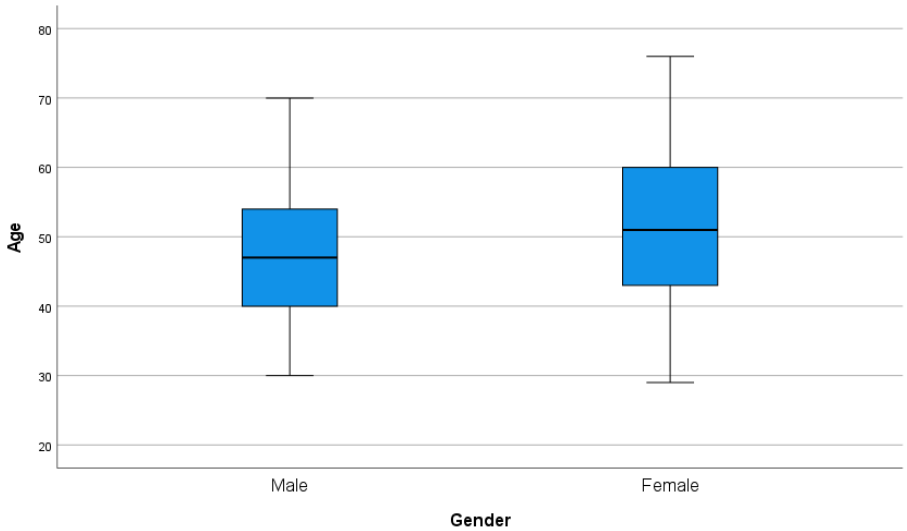

Figure 15. Distribution of age by sex

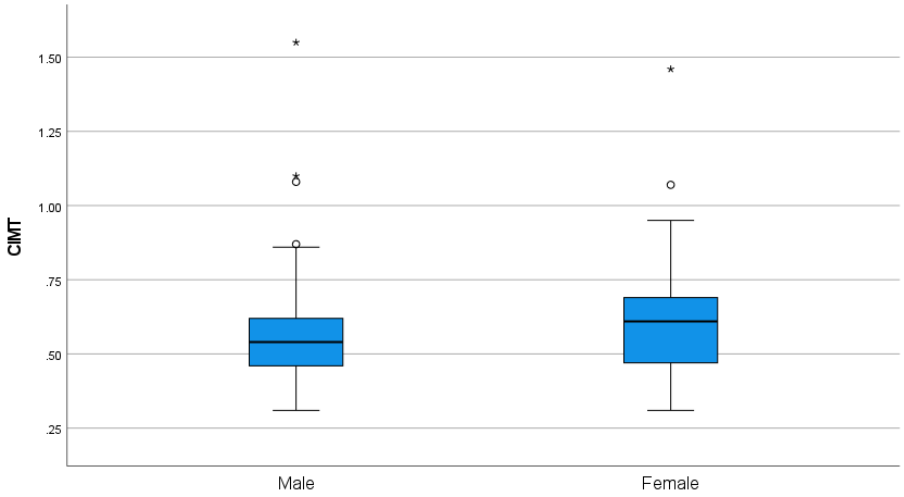

Figure 16. Comparison of CIMT by sex

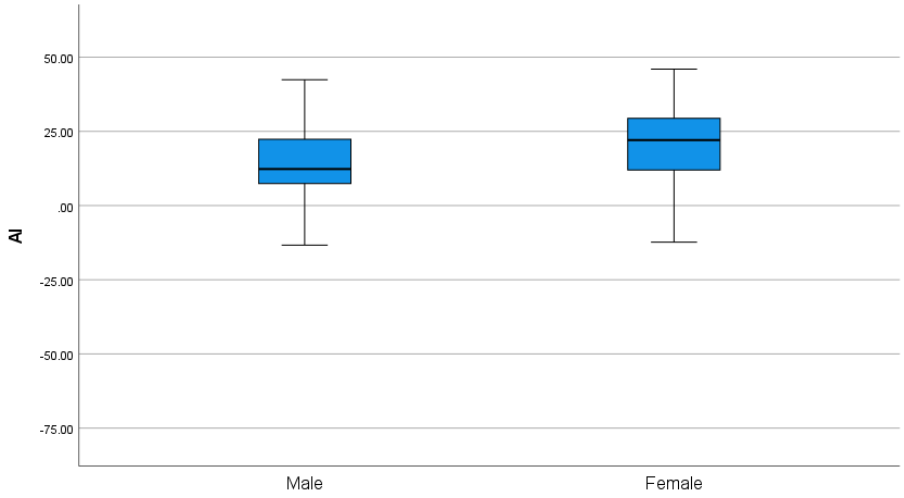

Figure 17. Comparison of augmentation index (AI) by sex

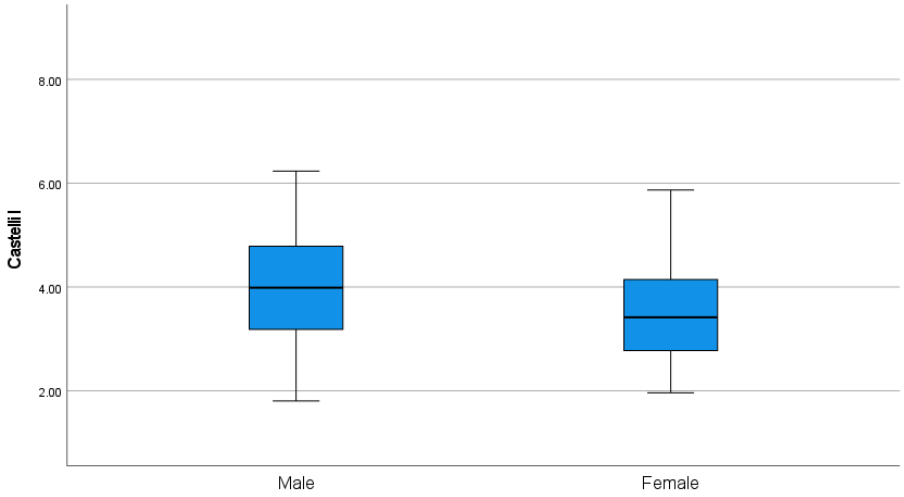

Figure 18. Comparison of Castelli I index by sex

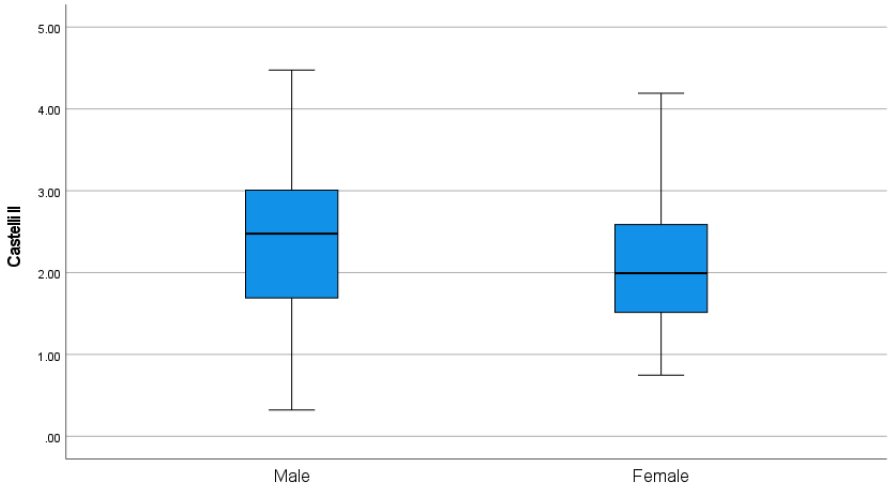

Figure 19. Comparison of Castelli II index by sex

16.4 Comparison by Smoking Status

No significant differences were found between groups in terms of smoking prevalence (χ^2 = **1.398, p = 0.497**). The proportion of smokers was similar across all groups: **55.4% in AS**, **65% in PsA**, and **64.5% in controls**.

When comparing smokers and non-smokers, a statistically significant difference was observed only for the **Framingham cardiovascular risk score (p = 0.018)**. This result is expected and consistent with the risk algorithms, in which smoking is an explicitly included predictor with strong prognostic weight.

However, no significant differences were found between smokers and non-smokers with respect to lipid profile, vascular ultrasound indices, inflammatory markers, or atherogenic indices. This lack of differences may be explained by the heterogeneity of the sample and the potential influence of confounding factors such as treatment, disease duration, and hypertension.

16.5 Comparison by Hypertension Status.

When comparing participants with and without arterial hypertension (HT), statistically significant differences were observed across several clinical, laboratory, and vascular parameters. Hypertensive patients demonstrated significantly higher levels of **ESR (p < 0.001)** and **CRP (p = 0.029)**, indicating a higher degree of systemic inflammatory activity.

Regarding vascular ultrasound indices of arterial stiffness, significant differences were identified in **CIMT (p = 0.005)**, **β-stiffness (p = 0.025)**, **augmentation index (AI) (p = 0.028)**, and **elastic modulus (Ep) (p = 0.045)**—all of which were elevated in hypertensive patients, reflecting more pronounced arterial rigidity in this subgroup (*Figures 20–23*).

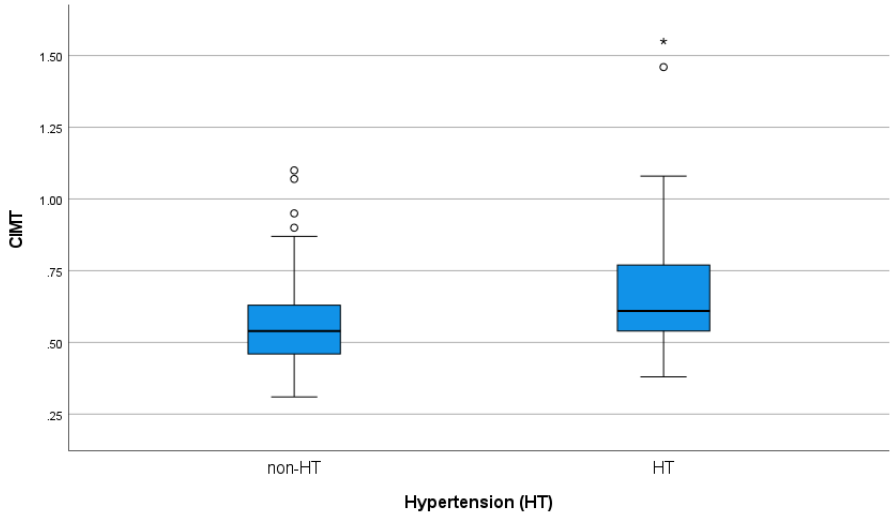

Figure 20. Comparison of carotid intima–media thickness (CIMT) in participants with and without hypertension

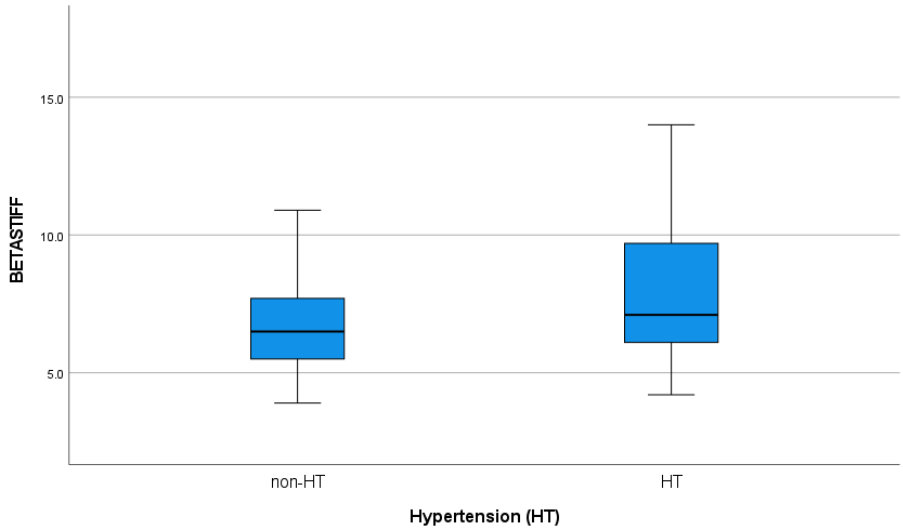

Figure 21. Comparison of β-stiffness in participants with and without hypertension

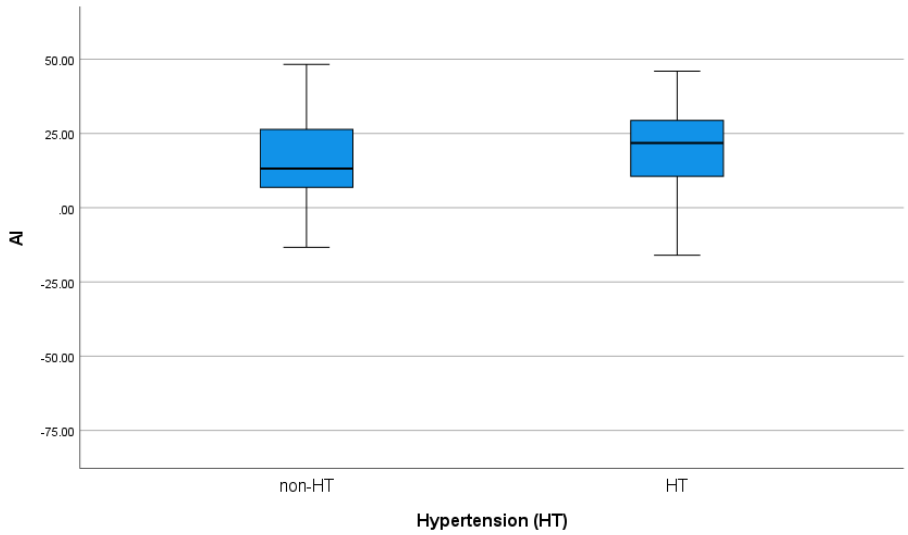

Figure 22. Comparison of augmentation index (AI) in participants with and without hypertension

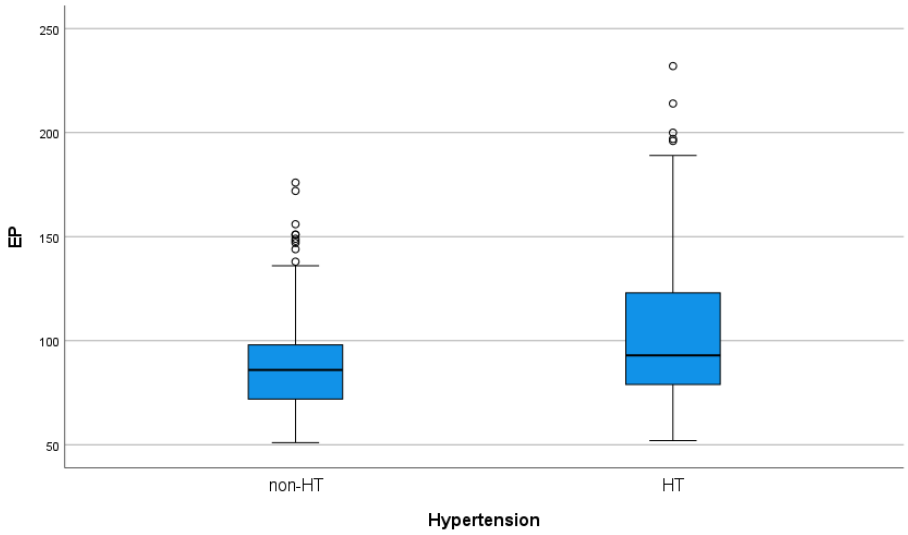

Figure 23. Comparison of elastic modulus (Ep) in participants with and without hypertension

Significant differences were also observed in **cardiovascular risk scores**—**Framingham (p = 0.002)** and **SCORE2 (p = 0.014)**—consistent with the inclusion of hypertension as a major determinant in these risk algorithms. In addition, **pulse pressure** was significantly higher in hypertensive patients (**p = 0.024**), serving as an additional indirect marker of arterial stiffness.

For the remaining studied parameters—including lipid profile, atherogenic indices, adhesion molecules (VCAM, ICAM), and anthropometric measures—no

statistically significant differences were detected between hypertensive and non-hypertensive participants.

16.6 Comparison by Disease Activity (BASDAI, ASDAS, DAS28)

For the purposes of analysis, participants with inflammatory arthropathies were stratified into subgroups according to disease activity using validated indices: **DAS28** for psoriatic arthritis (PsA) and **ASDAS** and **BASDAI** for ankylosing spondylitis (AS). Grouping followed accepted thresholds—**DAS28 ≤ 3.2** for controlled activity and **> 3.2** for moderate disease activity; **ASDAS ≤ 2.1** for low activity and **> 2.1** for high activity; **BASDAI < 4** vs **≥ 4**.

PsA (by DAS28). Statistically significant differences were identified for **mean arterial pressure (p = 0.007)**, with patients exhibiting higher disease activity being older and having higher mean arterial pressure. All other examined variables—including inflammatory markers, lipid profile, vascular ultrasound indices, atherogenic coefficients, cardiovascular risk scores, and adhesion molecules (ICAM, VCAM)—showed **no significant association** with DAS28 activity level.

AS (by ASDAS/BASDAI). Among AS patients stratified by disease activity, significant differences were observed in **CRP (p = 0.002)**, **ESR (p = 0.040)**, **β-stiffness (p = 0.032)**, and **VCAM (p = 0.002)** (*Figure 24*). The differences in CRP are expected, given its inclusion in ASDAS-CRP. These findings underscore the link between higher disease activity, systemic inflammation, and early changes in arterial stiffness and endothelial dysfunction (*Figure 25*).

For the remaining parameters—including lipid profile, **CIMT**, **PWV**, **AIP**, **SCORE**, **Framingham**, and anthropometric/hemodynamic variables—**no significant differences** were detected between AS patients with controlled versus active disease by ASDAS.

An additional activity analysis based on **BASDAI** revealed **no statistically significant differences** between controlled and active disease groups for any clinical,

laboratory, or vascular indices. This likely reflects the subjective nature of BASDAI and its lower sensitivity to objective biomarkers or vascular pathology.

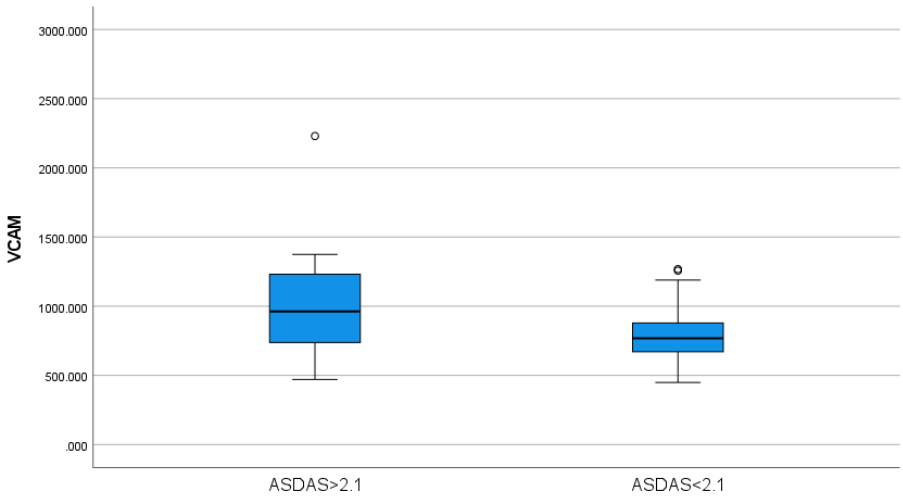

Figure 24. VCAM levels in AS patients by disease activity

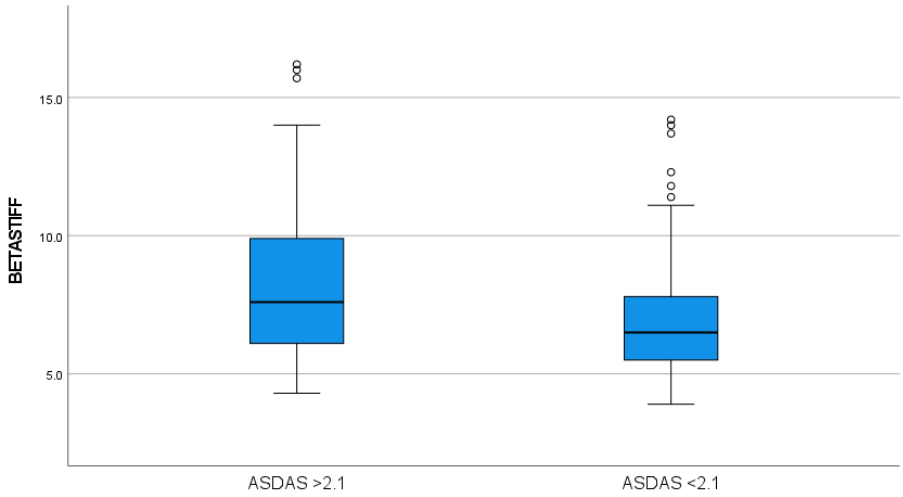

Figure 25. β-stiffness in AS patients by disease activity

16.7 Comparison by Therapy

A comparative analysis was conducted across major therapeutic subgroups in AS and PsA: **anti-TNF (n = 58)**, **IL-17 inhibitors**, **JAK inhibitors (n = 13)**, and **biologic-naïve** patients. In one-way nonparametric analysis (Kruskal–Wallis H test), **no statistically significant differences** were observed for most laboratory, inflammatory, and vascular indices. Exceptions included **treatment duration (p < 0.001)**—expected given the chronology of approval and adoption of different biologics—and **pulse pressure (p = 0.048)**, which differed significantly across subgroups. Several variables

showed borderline significance (e.g., **CRP**, **VCAM**, **SCORE2**, and **diastolic pressure**) without reaching conventional thresholds. Nevertheless, for exploratory purposes, pairwise analyses with the Mann–Whitney U test were performed in order to highlight potential trends between specific therapeutic strategies. The obtained results should be interpreted with caution and considered as hypothesis-generating.

A focused two-group comparison between **anti-TNF** and **JAK inhibitor** therapy (*Table 14*) showed **higher ESR (p = 0.050)** and **higher pulse pressure (p = 0.015)** in the anti-TNF group, despite **no significant differences** in principal arterial stiffness indices (**CIMT**, **β-stiffness**, **PWV**, **AI**, **ACo**, **Ep**). These results may reflect greater chronic inflammatory activity or a more advanced stage of vascular remodeling in the anti-TNF subgroup. Patients treated with JAK inhibitors had a **significantly shorter treatment duration (p = 0.017)**, aligning with their later introduction into clinical practice. Although not statistically significant, trends toward **lower VCAM (p = 0.187)**, **AI (p = 0.354)**, and **PWV (p = 0.106)** in JAK-treated patients could suggest favorable effects on endothelial function and arterial elasticity—hypotheses that warrant confirmation in larger cohorts with longitudinal follow-up.

Table 14. Comparison between patients on anti-TNF therapy and JAK inhibitors

Parameter	p-value	Mean rank (anti-TNF)	Mean rank (JAK)	Comment
PWV	0.015	38.73	23.81	Higher with anti-TNF
ESR	0.050	38.28	25.85	Higher with anti-TNF
Treatment duration	0.017	38.75	23.73	Longer with anti-TNF
VCAM	0.144	37.12	31.00	Trend toward higher with anti-TNF

No consistent linear relationships were found between **therapy type** and other variables in correlation analyses, which is expected since therapy is a categorical variable. It should be noted that the small number of patients on JAK inhibitors (**n = 13**) limits statistical power and increases the risk of type II error. Nevertheless, the differences in pulse pressure and ESR, together with trends in vascular parameters,

support the hypothesis of potentially distinct inflammatory and vascular profiles across therapeutic subgroups.

An additional two-group comparison between **biologic-naïve** patients (**n = 20**) and those treated with **anti-TNF** (**n = 58**) (*Table 15*) revealed significant differences in **disease duration (p < 0.001)** and **pulse pressure (p = 0.041)**—both higher in anti-TNF-treated patients. This likely reflects a more advanced disease stage among biologically treated individuals and possible accumulation of subclinical vascular changes despite therapy.

Regarding **VCAM**, a marker of endothelial dysfunction and vascular activation, **significantly higher values** were observed in biologic-naïve patients (**p = 0.046**), which may indicate a favorable effect of TNF blockade on endothelial activation. Similarly, **SCORE2** values were higher in the naïve group (**p = 0.020**), suggesting a cumulatively higher cardiovascular risk in these patients.

Table 15. Comparison between anti-TNF–treated and biologic-naïve patients

Parameter	p-value	Mean rank: anti-TNF	Mean rank: naïve	Comment
Pulse pressure	0.041	42.48	30.85	Significantly higher with anti-TNF
Disease duration	<0.001	44.95	22.23	Significantly longer with anti-TNF
VCAM	0.046	36.50	48.20	Significantly higher in naïve
SCORE2	0.020	32.40	39.58	Higher CV risk in naïve

Despite statistical significance in some parameters, no correction for multiple comparisons was applied, and the size of the biologic-naïve subgroup remains relatively small. This limits statistical power and warrants cautious interpretation—these results may indicate an effect of anti-TNF therapy on vascular and inflammatory profiles.

A comparison between **JAK inhibitor**–treated patients and **biologic-naïve** patients (*Table 16*) showed a **significant difference in treatment duration (p < 0.001)**, consistent with the more recent adoption of JAK inhibitors. No other parameter

reached statistical significance, though several trends were noted. **Mean arterial pressure** tended to be higher in biologic-naïve patients (p = 0.194), potentially reflecting greater vascular stiffness. **SCORE** was higher in the JAK group (p = 0.437), but without statistical significance. The most notable finding concerned **VCAM-1**: patients on JAK inhibitors had **significantly lower VCAM-1** than biologic-naïve patients (**p = 0.014**), supporting a potential anti-inflammatory and vasculoprotective effect of JAK inhibitors.

In the comparison between **anti-IL-17** therapy and **biologic-naïve** patients, treatment duration again differed significantly (**p < 0.001**), as expected. **VCAM-1** showed a trend toward higher values in biologic-naïve patients (**p = 0.063**), suggesting a possible beneficial effect of IL-17 inhibition on endothelial function, although statistical significance was not reached. Cardiovascular risk scores did not differ significantly—**SCORE** was numerically higher in anti-IL-17–treated patients (**p = 0.403**), and mean arterial pressure was higher in the naïve group (**p = 0.400**), both without significance.

Although many comparisons did not reach statistical significance, the observed trends in **VCAM-1** and in blood pressure and cardiovascular risk indices suggest possible effects of biologic therapy on vascular function and risk that merit further investigation in larger, longitudinal cohorts.

Table 16. Comparison between patients on JAK inhibitors and biologic-naïve patients

Parameter	p-value	Mean rank (JAK)	Mean rank (Naïve)	Comment
Treatment duration	<0.001	11.92	20.30	Shorter with JAK
VCAM	0.014	11.92	20.30	Lower with JAK
Mean arterial pressure	0.194	14.27	18.77	Trend toward lower with JAK
SCORE	0.437	13.85	11.54	Not significant

A comparison between **anti-TNF (n = 58)** and **anti-IL-17 (n = 32)** revealed several significant differences. **CRP** levels were higher in the anti-TNF group (**p = 0.015**), potentially reflecting differences in inflammatory profile or disease stage. A similar difference was observed for **ASDAS-CRP (p = 0.032)**, supporting higher disease activity in the anti-TNF subgroup. Significant differences were also seen for **triglycerides (p = 0.049)** and **AIP (p = 0.028)**, both higher with anti-TNF therapy, suggesting a potentially less favorable lipid profile. Other indices—including **VCAM (p = 0.873)**, **ICAM (p = 0.781)**, **pulse pressure (p = 0.273)**, and **mean arterial pressure (p = 0.413)**—did not differ significantly. Cardiovascular risk scores likewise showed **no significant variation—SCORE2 (p = 0.200)** and **Framingham (p = 0.375)**—indicating no substantive difference in overall CV risk between these therapeutic strategies.

An additional comparison between **anti-IL-17** and **JAK inhibitors** identified a significant difference only in **treatment duration (p = 0.005)**, with shorter exposure to JAK inhibitors, consistent with their later clinical introduction. No substantial differences in inflammatory activity were observed; although **CRP** tended to be higher with JAK inhibitors (**p = 0.239**), this did not reach significance, and similar results were seen for **ESR**. Lipid profile trends toward higher **triglycerides (p = 0.282)**, **AIP (p = 0.127)**, and **non-HDL cholesterol (p = 0.401)** with JAK inhibitors were not statistically significant, but they suggest a potentially less favorable metabolic effect warranting further study. No significant differences emerged in vascular ultrasound indices (**CIMT**, **β-stiffness**, **AI**, **PWV**, **ACo**, **Ep**), adhesion molecules (**ICAM**, **VCAM**), or cardiovascular risk scores. Although β-stiffness, AI, and PWV were slightly higher with anti-IL-17 therapy, all **p > 0.3**.

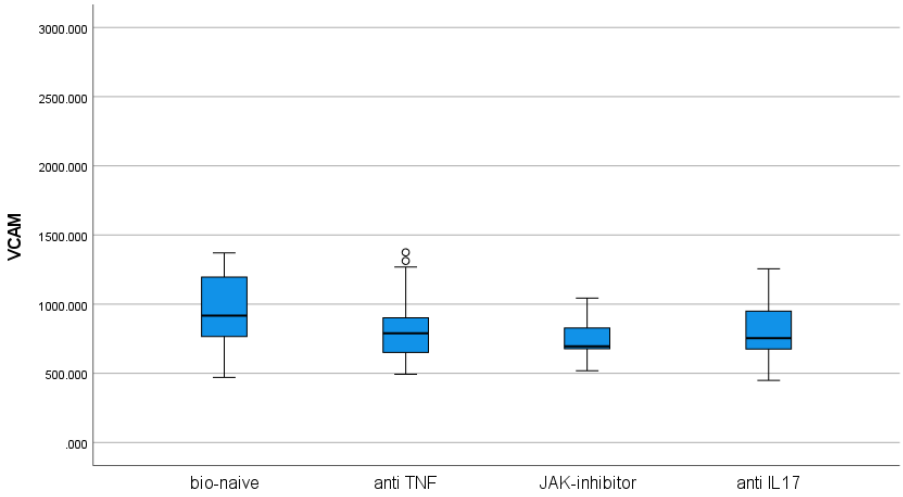

Figure 26. Distribution of VCAM-1 values by therapeutic subgroup (biologic-naïve, anti-TNF, JAK inhibitors, anti-IL-17)

17. Correlation Analysis Between Parameters

17.1 Correlations between Ultrasonographic Vascular Indices and Other Determinants of Cardiovascular Risk

Correlation analysis between demographic characteristics and ultrasonographic indices of arterial stiffness revealed several significant associations. **Age** showed a statistically significant positive correlation with all key ultrasound parameters—including **elastic modulus (EP)** (rho = 0.458, $p < 0.001$), **carotid intima–media thickness (CIMT)** (rho = 0.494, $p < 0.001$) (*Figure 27*), **β-stiffness** (rho = 0.445, $p < 0.001$) (*Figure 28*), and **pulse wave velocity (PWV)** (rho = 0.424, $p < 0.001$) (*Figure 29*). These findings confirm the expected progressive increase in arterial stiffness with advancing age.

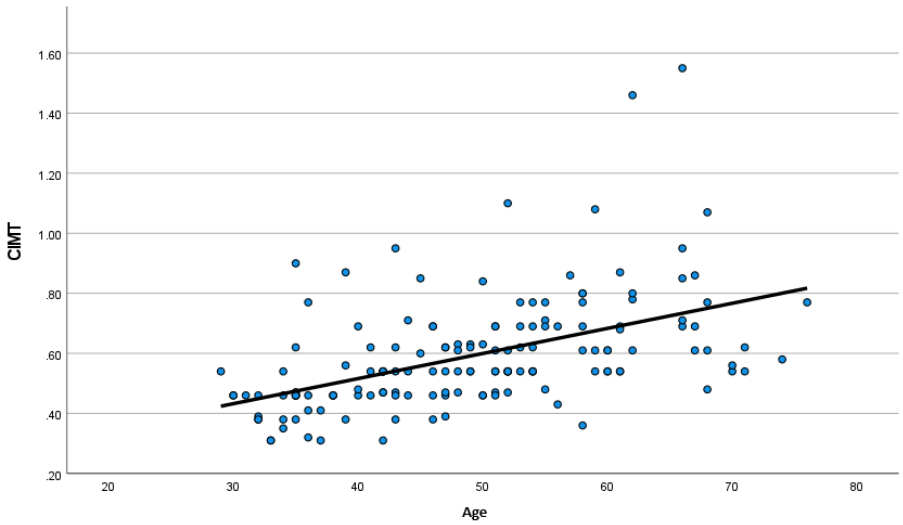

Figure 27. Correlation between age and CIMT (rho = 0.419, p < 0.001).

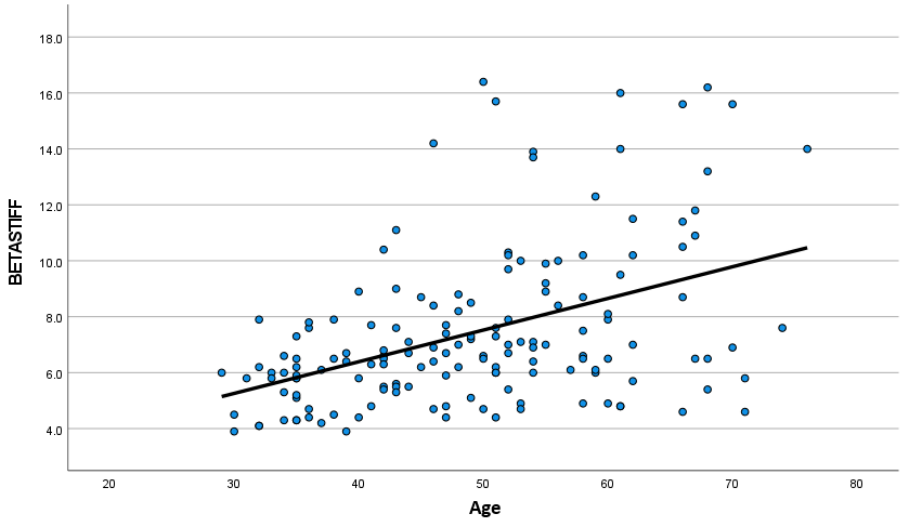

Figure 28. Correlation between age and β-stiffness (rho = 0.609, p < 0.001).

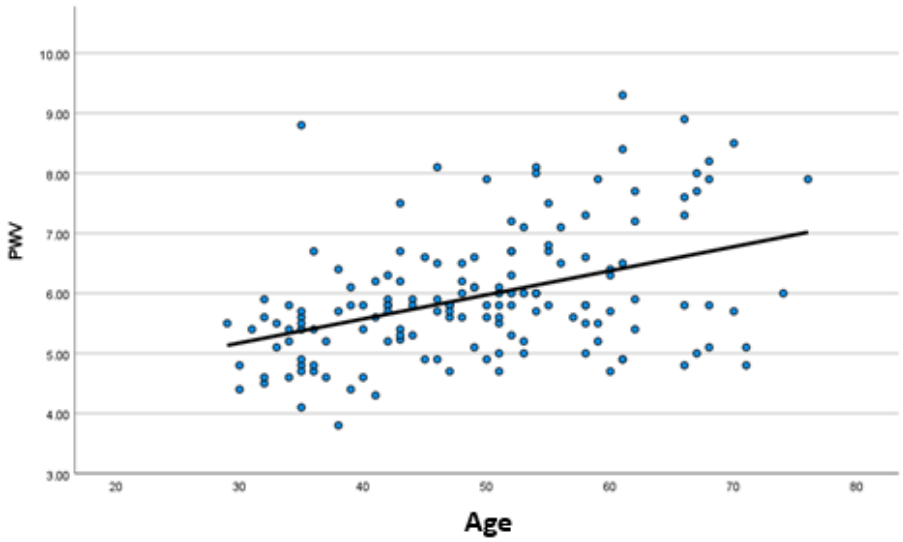

Figure 29. Correlation between age and PWV (r = 0.529, p < 0.001).

Arterial hypertension also correlated positively with **EP** (rho = 0.209, p = 0.009), **CIMT** (rho = 0.234, p = 0.003), and **β-stiffness** (rho = 0.227, p = 0.005), reflecting the well-recognized role of hypertension in accelerating structural changes of the arterial wall. **Sex** did not exert a substantial influence on vascular parameters, except for a weak correlation with **ACo** (rho = –0.160, p = 0.047) and with **age** (rho = 0.190, p = 0.018), likely reflecting age differences between men and women in the sample. **Smoking** was not associated with significant changes in the measured indices, probably due to homogeneity among participants. In summary, **age** and **hypertension** emerge as leading demographic determinants of increased arterial stiffness in this cohort.

17.2 Correlations between Lipid Fractions and Ultrasonographic Vascular Indices

Correlation analysis between lipid fractions and vascular ultrasound parameters identified several weak but statistically significant relationships. Most notably, there was a positive correlation between **total cholesterol** and **CIMT** (rho = 0.159, p = 0.048), and between **triglycerides (TG)** and **CIMT** (rho = 0.172, p = 0.033) (*Figure 30*), suggesting that elevated serum lipids may be linked to arterial wall thickening—a marker of subclinical atherosclerosis. **LDL-cholesterol** showed a weak positive association with CIMT (rho = 0.076, p = 0.349) that did not reach significance, while **HDL-cholesterol** demonstrated no meaningful relationship with CIMT (rho = –0.046, p = 0.568).

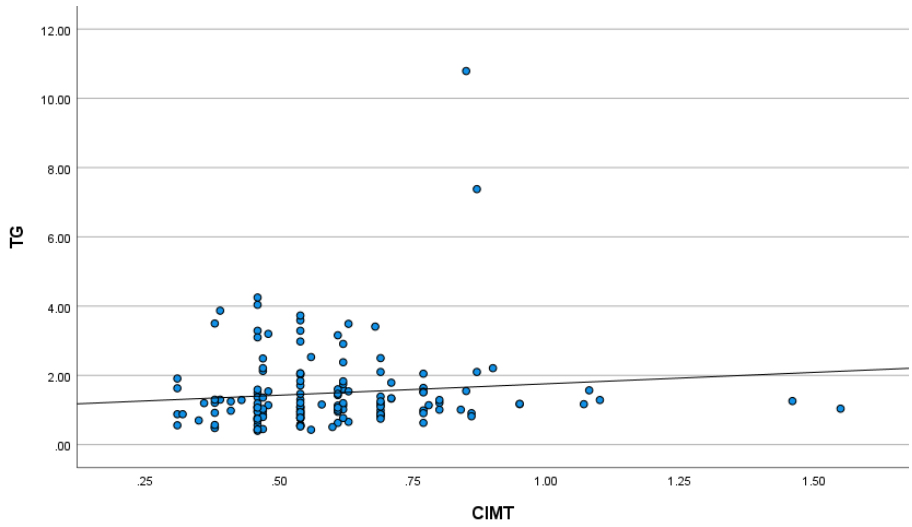

Figure 30. Visualization of the correlation between CIMT and serum triglycerides (TG).

Regarding functional stiffness parameters, the clearest trends were observed between **triglycerides** and **β-stiffness** (rho = 0.150, p = 0.063) and between **triglycerides** and **EP** (rho = 0.154, p = 0.056), both bordering on statistical significance. **LDL** did not correlate significantly with any stiffness indices, whereas **HDL** showed a weak but statistically significant **negative** correlation with the **augmentation index (AI)** (rho = –0.197, p = 0.014), consistent with HDL's cardioprotective role. Overall, **triglycerides** exhibited the strongest links—albeit weak—with both structural and functional vascular indices, while total and LDL cholesterol showed weaker and partly nonsignificant associations. These data align with literature highlighting **hypertriglyceridemia** as an indicator of vascular damage and reinforce **CIMT** as a sensitive marker of lipid-mediated subclinical atherosclerosis.

Among composite lipid indices, **Castelli I** did not show significant relationships with any ultrasound measures (CIMT, β-stiffness, AI, PWV, ACo, EP). Similarly, **Castelli II** was not significantly associated with vascular indices (all p > 0.05).

In contrast, the **Atherogenic Coefficient** showed a tendency toward positive correlation with **CIMT** (rho = 0.140, p = 0.082) and **β-stiffness** (rho = 0.156, p = 0.053), though both fell short of statistical significance. No significant associations were found with AI, PWV, ACo, or EP.

Table 17. Spearman correlations between lipid parameters and vascular ultrasound indices

Lipid parameter	Vascular index	Spearman ρ	p-value

Total cholesterol	CIMT	0.159	0.048
Triglycerides	CIMT	0.172	0.033
LDL-cholesterol	CIMT	0.076	0.349
HDL-cholesterol	CIMT	–0.046	0.568
Triglycerides (TG)	β-stiffness	0.150	0.063
Triglycerides (TG)	EP	0.154	0.056
HDL-cholesterol	AI	–0.197	0.014
Castelli I	HDL	–0.235	0.003
Atherogenic Coefficient	CIMT	0.140	0.082
Atherogenic Coefficient	β-stiffness	0.156	0.053
Atherogenic Index of Plasma (AIP)	β-stiffness	0.150	0.063
Atherogenic Index of Plasma (AIP)	EP	0.143	0.078

The **Atherogenic Index of Plasma (AIP)** did not show statistically significant relationships with vascular ultrasound parameters, though small positive trends were noted with **β-stiffness** (rho = 0.150, p = 0.063) and **EP** (rho = 0.143, p = 0.078).

In summary, lipid indices in this study did not display strong correlations with structural and functional arterial wall parameters. The closest to significance were **CIMT** and **β-stiffness** versus the **Atherogenic Coefficient** and **AIP**, suggesting that although atherogenic indices are established markers of cardiovascular events, their direct reflection in ultrasound markers of arterial stiffness may be limited in a population with inflammatory arthropathies.

17.3 Correlation Between Ultrasound Parameters

The analysis of the associations between carotid intima-media thickness (CIMT) and other ultrasound vascular parameters demonstrated statistically significant positive correlations with all major functional indices of arterial stiffness (Table 18). The strongest correlation was observed between CIMT and pulse wave velocity (PWV) (rho = 0.528, p < 0.001) (Figure 32), followed by associations with β-stiffness (rho = 0.500, p < 0.001) (Figure 31) and with elastic modulus (EP) (rho = 0.520, p < 0.001) (Figure 33). These findings indicate that increased arterial wall thickness is

accompanied by reduced vascular elasticity, as reflected by functional vascular indices. This supports the concept that CIMT is not only a morphological indicator of early arteriosclerosis but is also associated with measurable alterations in vascular function.

Table 18. Correlations between carotid intima-media thickness (CIMT) and functional ultrasound parameters of arterial stiffness

Other vascular parameters	Ultrasound indices of arterial stiffness	Spearman rho	p-value
CIMT	PWV	0.528	<0.001
CIMT	β-stiffness	0.500	<0.001
CIMT	EP	0.520	<0.001
CIMT	AI	0.208	0.010

A weaker but still statistically significant correlation was found between CIMT and the augmentation index (AI) (rho = 0.208, p = 0.010), suggesting that AI is directly influenced by arterial morphology in the studied population.

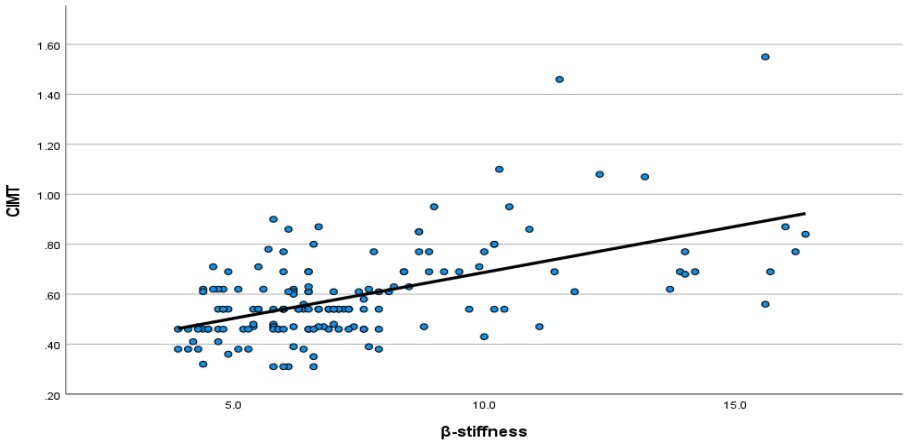

Figure 31. Correlation between CIMT and β-stiffness (rho = 0.500, p < 0.001).

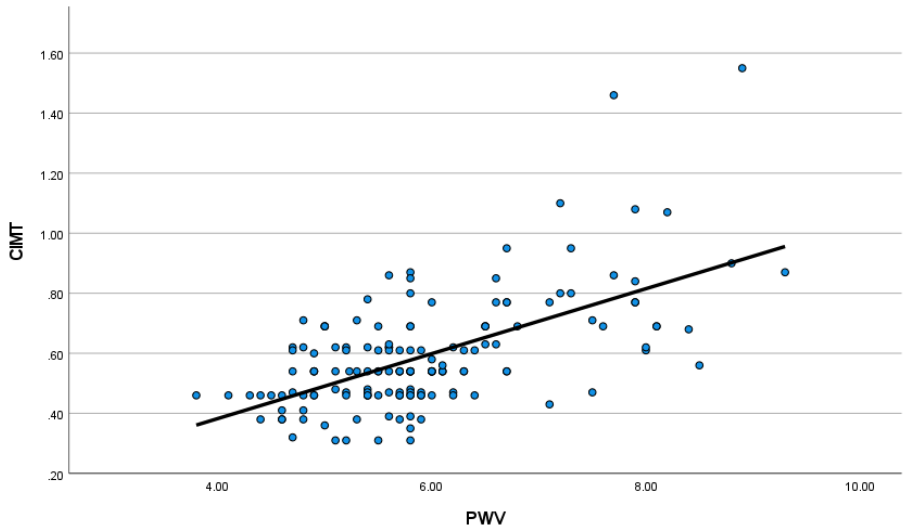

Figure 32. Correlation between CIMT and PWV (rho = 0.528, p < 0.001).

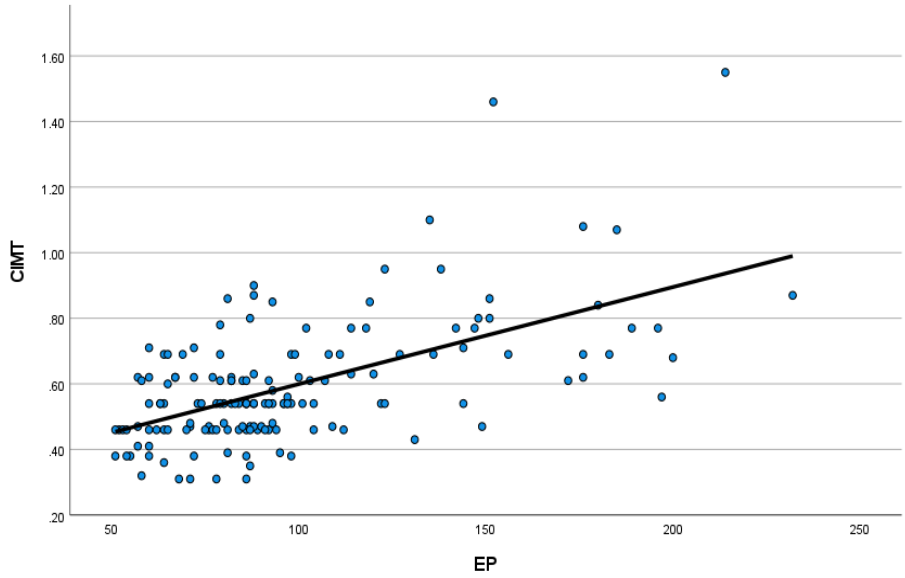

Figure 33. Correlation between CIMT and elastic modulus (EP) (rho = 0.520, p < 0.001).

17.4 Correlation Analysis Between Ultrasound Parameters and Cardiovascular Risk Scores

The analysis of the associations between ultrasound vascular indices and established cardiovascular risk scores revealed several statistically significant correlations (Table 19). Cardiovascular risk assessment using the Framingham and SCORE2 scales did not show significant differences between patients with ankylosing spondylitis (AS), psoriatic arthritis (PsA), and the control group (Kruskal–Wallis: Framingham p = 0.648; SCORE2 p = 0.146) (Figures 8–9).

With respect to their relationship to vascular parameters, SCORE2 demonstrated a weak but significant positive correlation with CIMT (rho = 0.239, p = 0.003), while no associations were observed with β-stiffness, PWV, EP, or ACo (all p > 0.05). The Framingham score did not correlate significantly with CIMT or with the indices of arterial stiffness (p > 0.05). These findings suggest that in this cohort, SCORE2 partly reflects structural vascular changes (through CIMT), whereas indices of arterial stiffness do not show independent associations with the risk scores used.

Table 19. Correlations between ultrasound vascular parameters and cardiovascular risk scores (Framingham and SCORE2)

Parameter	Rho (SCORE2)	p (SCORE2)	Rho (Framingham)	p (Framingham)
CIMT	0.239	0.003	0.060	0.463
β-stiffness	0.064	0.439	0.010	0.903
PWV	0.101	0.220	0.027	0.735
EP	0.115	0.164	0.049	0.549
ACo	–0.101	0.220	0.059	0.468

17.5 Correlations Between Ultrasound Vascular Indices and Disease Activity

The analysis of correlations between ultrasound vascular indices and disease activity scores (ASDAS-CRP, BASDAI, and DAS28) revealed limited associations between these variables. No statistically significant correlations were observed between any of the ultrasound vascular indices and the composite activity score ASDAS-CRP (p > 0.05), suggesting that vascular changes assessed by CIMT, β-stiffness, PWV, arterial compliance (ACo), and elastic modulus (EP) do not directly reflect current inflammatory burden according to this objective index.

When evaluating subjective disease activity in ankylosing spondylitis using BASDAI, a statistically significant but weak negative correlation was observed with arterial compliance (rho = –0.231, p = 0.029). This finding suggests that higher subjective disease activity may be associated with reduced vascular elasticity and

increased stiffness. Other vascular parameters did not show significant associations with BASDAI, limiting the generalizability of this observation.

Regarding DAS28, used to assess disease activity in psoriatic arthritis, no statistically significant correlations were found with any of the studied ultrasound vascular indices ($p > 0.05$). These results indicate that vascular stiffness and CIMT are not substantially correlated with clinical disease activity as measured by this tool.

17.6 Correlations Between Ultrasound Vascular Indices and Inflammatory Markers

The analysis of associations between ultrasound vascular parameters and laboratory markers of inflammation (ESR and CRP) revealed some statistically significant but predominantly weak correlations. Among the five vascular indices, arterial compliance (ACo) showed a significant negative correlation with ESR values ($rho = –0.185$, $p = 0.022$), suggesting that higher levels of inflammation are associated with reduced vascular elasticity.

The remaining vascular parameters – CIMT, β-stiffness, PWV, and EP – did not show significant associations with CRP or ESR ($p > 0.05$). This suggests that although inflammation may exert some influence on vascular function, the effect is likely indirect or modulated by other factors, such as disease chronicity, therapy, and individual vascular status.

17.7 Correlation Analysis of Adhesion Molecules ICAM and VCAM

The correlation analysis showed that intercellular adhesion molecule-1 (ICAM-1) did not demonstrate statistically significant associations with most of the examined clinical, laboratory, and ultrasound parameters. Nevertheless, a positive correlation was observed between ICAM-1 and VCAM-1 ($rho = 0.291$, $p < 0.001$), which is expected given their shared role in endothelial dysfunction and leukocyte adhesion. Beyond this relationship, ICAM-1 did not exhibit significant correlations with lipid

profile, atherogenic indices, arterial stiffness markers, or measures of inflammatory activity. All other associations with variables such as CRP, ESR, CIMT, β-stiffness, AI, PWV, AIP, SCORE2, and Framingham were weak and statistically non-significant ($p > 0.05$).

In contrast, vascular cell adhesion molecule-1 (VCAM-1) demonstrated a broader range of significant correlations with parameters reflecting both inflammatory activity and subclinical atherosclerosis. A positive correlation was found between VCAM-1 and ESR (rho = 0.163, p = 0.044), as well as with CRP (rho = 0.247, p = 0.002) (Figure 33), suggesting a potential link between endothelial dysfunction and systemic inflammation.

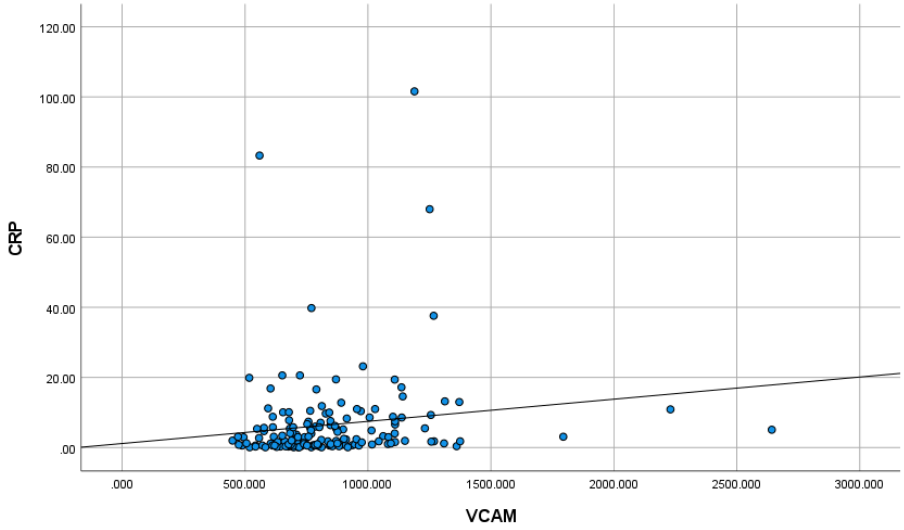

Figure 33. Correlation between VCAM-1 and CRP in the studied cohort

With respect to ultrasound indices, no statistically significant associations were observed with CIMT, β-stiffness, AI, PWV, or EP. However, VCAM-1 was significantly correlated with SCORE2 (rho = 0.305, p = 0.001). There were no statistically significant correlations between the lipid parameters and the adhesion molecules.Although no significant associations were identified between VCAM-1 and specific ultrasound indices of arterial stiffness (e.g., β-stiffness, PWV, AI), its combined correlations with inflammatory markers and atherogenic indices highlight the multifactorial pathophysiological role of VCAM-1. This likely reflects not only structural vascular alterations but also functional endothelial activation related to

systemic inflammation and metabolic disturbances in patients with inflammatory arthropathies.

Table 20. Correlations of ICAM-1 and VCAM-1 with clinical, laboratory, and vascular parameters (Spearman's rho and p-values)

Parameter	rho (ICAM)	p (ICAM)	rho (VCAM)	p (VCAM)
ESR	–0.032	0.697	0.163	0.044
CRP	0.093	0.254	0.247	0.002
Total cholesterol	–0.058	0.473	–0.126	0.118
LDL	–0.042	0.603	–0.065	0.425
HDL	–0.083	0.309	–0.156	0.054
Triglycerides	–0.042	0.603	–0.018	0.828
Non-HDL cholesterol	–0.028	0.729	–0.062	0.448
Atherogenic coefficient	0.072	0.378	0.039	0.635
AIP	–0.063	0.440	0.009	0.910
Castelli I	0.158	0.051	0.095	0.241
Castelli II	0.149	0.065	0.122	0.132
CIMT	0.085	0.295	0.065	0.424
β-stiffness	0.119	0.142	0.111	0.172
AI	0.056	0.489	0.086	0.291
PWV	0.076	0.349	0.058	0.479
ACo	–0.014	0.865	–0.108	0.182
EP	0.084	0.298	0.063	0.439
Framingham	0.089	0.277	–0.014	0.861

17.8 Correlation Analysis between Lipid Profile, Atherogenic Indices, and Cardiovascular Risk Scores

The correlation analysis between lipid parameters, atherogenic indices, and cardiovascular risk scores revealed statistically significant associations, as expected given the inclusion of lipid components in the risk calculation algorithms. The **Framingham risk score** correlated positively with total cholesterol ($p = 0.003$),

triglycerides ($p = 0.001$), LDL ($p = 0.003$), the atherogenic coefficient ($p < 0.001$), and AIP ($p = 0.002$), while showing an inverse correlation with HDL ($p = 0.002$).

Among the composite indices, **AIP** exhibited strong positive associations with triglycerides ($p < 0.001$), LDL ($p = 0.031$), and total cholesterol ($p = 0.040$), along with a negative correlation with HDL ($p < 0.001$). Moreover, AIP was very strongly correlated with the atherogenic coefficient ($p < 0.001$). **Castelli I and II indices** were also significantly intercorrelated ($p < 0.001$) and demonstrated associations with the atherogenic coefficient ($p = 0.001$ and $p < 0.001$, respectively) as well as with HDL ($p = 0.003$ and $p < 0.001$, respectively). These findings are consistent with their mathematical formulations and support their established clinical utility as indicators of lipid-related cardiovascular risk.

17.9 Correlation Analysis between Inflammatory Markers (CRP and ESR) and Atherogenic Indices

The evaluation of correlations between inflammatory and lipid parameters (Table 21) revealed a statistically significant negative correlation between CRP and HDL cholesterol (rho = –0.271; $p = 0.001$), as well as between ESR and HDL (rho = –0.189; $p = 0.019$). These findings are consistent with the well-established effect of inflammation in lowering the levels of the anti-atherogenic HDL fraction.

In addition, CRP showed a weak negative correlation with total cholesterol (rho = –0.163; $p = 0.044$), but no significant associations with LDL ($p = 0.171$) or triglycerides (rho = 0.125, $p = 0.123$). ESR did not demonstrate statistically significant correlations with total cholesterol, triglycerides, or LDL (all $p > 0.05$). These results emphasize that chronic inflammation primarily affects HDL cholesterol, whereas associations with other lipid parameters are weaker and statistically less consistent.

Table 21. Correlations between inflammatory markers (CRP and ESR) and lipid profile

Parameter	Total cholesterol (Spearman rho)	p-value	TG (Spearman rho)	p-value	LDL (Spearman rho)	p-value	HDL (Spearman rho)	p-value
CRP	–0.163	0.044	0.125	0.123	–0.111	0.171	–0.271	0.001
ESR	–0.144	0.075	0.060	0.461	–0.057	0.486	–0.189	0.019

17.10 Correlations between Disease Activity Indices and Lipid, Vascular, and Cardiovascular Risk Profiles

Analysis of the associations between disease activity indices and metabolic or vascular parameters revealed several statistically significant correlations. The ASDAS-CRP index showed strong positive correlations with ESR (rho = 0.529, $p < 0.001$), CRP (rho = 0.676, $p < 0.001$), and BASDAI (rho = 0.773, $p < 0.001$), confirming its validity as a composite measure of inflammatory activity. In addition, ASDAS-CRP demonstrated a weak negative correlation with total cholesterol (rho = –0.240, p = 0.023) and a weak positive correlation with pulse pressure (rho = 0.246, p = 0.020), but no significant associations with vascular ultrasound indices.

The BASDAI index did not show statistically significant associations with any of the examined lipid, vascular, or cardiovascular parameters, likely reflecting its more subjective nature.

By contrast, in patients with psoriatic arthritis, the DAS28 index correlated positively with the atherogenic index AIP (rho = 0.246; p = 0.024), suggesting a possible link between higher disease activity and a pro-atherogenic lipid profile. Furthermore, DAS28 was positively associated with carotid intima-media thickness (CIMT) (rho = 0.267; p = 0.011) and elastic modulus (EP) (rho = 0.265; p = 0.012). A significant positive correlation was also observed between DAS28 and the SCORE2 cardiovascular risk index (rho = 0.319; p = 0.015), underscoring the clinical relevance of active inflammation as a modifiable risk factor.

In contrast, analysis of correlations between inflammatory markers (CRP and ESR) and established cardiovascular risk scores (Framingham and SCORE2) revealed no statistically significant associations. The SCORE2 index showed only a borderline positive correlation with ESR (rho = 0.160, p = 0.053), which did not reach statistical significance, while the correlation with CRP was weak and nonsignificant (rho = 0.054, p = 0.516). The Framingham score did not demonstrate significant associations with either ESR (rho = –0.024, p = 0.770) or CRP (rho = 0.064, p = 0.430), consistent with the fact that this model does not include inflammatory markers in its calculation formula.

17.11 Correlations between Disease Activity, Vascular Parameters, and Markers of Endothelial Dysfunction in Patients with Ankylosing Spondylitis

Correlation analysis in the group of patients with ankylosing spondylitis revealed important associations between disease activity (assessed by ASDAS-CRP and BASDAI), structural and functional vascular parameters, and levels of adhesion molecules (VCAM and ICAM). These findings illustrate the multidisciplinary nature of inflammatory vascular pathology in this population.

Analysis of correlations between disease duration and various clinical, biochemical, and ultrasound parameters revealed significant associations, emphasizing the cumulative impact of chronic inflammation and metabolic alterations on vascular health.

Age emerged as a strongly associated factor with several measures of vascular damage and cardiovascular risk in patients with ankylosing spondylitis. Statistically significant positive correlations were observed between age and the main ultrasound vascular parameters. The strongest association was with carotid intima-media thickness (CIMT) (rho = 0.618; p = 0.001). Similarly, age showed a strong positive correlation with pulse wave velocity (PWV) (rho = 0.630; p < 0.001), reflecting progressive arterial stiffness with increasing age.

Significant associations were also found with cardiovascular risk scores. SCORE2 demonstrated the highest correlation with age (rho = 0.765; $p < 0.001$), followed by the Framingham score (rho = 0.681; $p < 0.001$), which is fully expected given the built-in role of age as a prognostic factor in these algorithms. Additionally, age correlated positively with the elastic modulus (EP) (rho = 0.520; $p < 0.001$) and with β-stiffness (rho = 0.492; $p < 0.001$), underscoring the overall trend toward reduced vascular elasticity and increased vascular resistance in older patients.

No statistically significant correlations were found between age and inflammatory markers or disease activity indices. This suggests that age plays a greater role in determining vascular and metabolic status than in influencing the current inflammatory activity of the disease.

Regarding the lipid profile, positive trends were observed between age and LDL, non-HDL cholesterol, and atherogenic indices, although most did not reach statistical significance. These findings reinforce the concept that, in patients with ankylosing spondylitis, advancing age is accompanied by both structural vascular changes and metabolic alterations, contributing to increased cardiovascular risk.

Disease duration demonstrated statistically significant positive correlations with key ultrasound vascular parameters. The strongest correlation was with CIMT (rho = 0.498; $p = 0.004$). Similar positive correlations were observed with β-stiffness (rho = 0.467; $p = 0.007$), PWV (rho = 0.485; $p = 0.005$), and EP (rho = 0.453; $p = 0.008$). These findings clearly indicate that longer disease duration is associated with both structural vascular changes and functional deterioration of arterial elasticity. Elevated CIMT and PWV reflect the cumulative effect of inflammation and metabolic disturbances on the arterial wall, consistent with the concept of accelerated vascular aging in chronic inflammatory diseases.

In addition, disease duration correlated significantly with certain components of the lipid profile. The most notable correlations were with LDL cholesterol (rho = 0.402; $p = 0.020$), non-HDL cholesterol (rho = 0.388; $p = 0.024$), and the atherogenic

coefficient (total cholesterol/HDL) (rho = 0.406; p = 0.035). These associations reflect a trend toward worsening lipid metabolism in patients with longer disease duration, likely due to both chronic inflammation and the side effects of some therapeutic regimens. A weak negative correlation was also observed between disease duration and HDL cholesterol (rho = –0.180; p = 0.398), supporting the presence of lipoprotein profile remodeling toward increased atherogenic risk.

As a primary structural ultrasound parameter, CIMT (carotid intima-media thickness) showed significant positive correlations with all major indices of arterial stiffness (Table 22): β-stiffness (rho = 0.492; p < 0.001), PWV (rho = 0.553; p < 0.001), and EP (rho = 0.520; p < 0.001).

Table 22. Correlations between CIMT and other indices of arterial stiffness in patients with ankylosing spondylitis (Spearman rho)

Parameter	β-stiffness	PWV	EP	AI
CIMT	rho = 0.492 (p < 0.001)	rho = 0.553 (p < 0.001)	rho = 0.520 (p < 0.001)	rho = 0.073 (p = 0.510)

Additionally, although not statistically significant, CIMT showed a weak positive correlation with AI (rho = 0.073; p = 0.510). These results emphasize that intima thickening is associated with impaired vascular elasticity and stiffness, reflecting early subclinical atherosclerotic processes in patients with ankylosing spondylitis.

Analysis of cardiovascular risk scores also revealed important associations with vascular parameters (Table 23), independent of lipid profile. The Framingham score showed significant positive correlations with CIMT (rho = 0.438; p < 0.001), β-stiffness (rho = 0.314; p = 0.004), and EP (rho = 0.364; p = 0.001), while a moderate association was also observed with PWV (rho = 0.326; p = 0.003). Correlations with ACo (rho = –0.071; p = 0.526) and AI (rho = –0.014; p = 0.901) were weak and nonsignificant.

The SCORE2 index, however, demonstrated significant positive associations with CIMT (rho = 0.488; p < 0.001) and β-stiffness (rho = 0.289; p = 0.025), as well as a positive correlation with EP (rho = 0.215; p = 0.099), though the latter did not reach statistical significance. This confirms that the European SCORE2 model has the potential to reflect vascular changes associated with subclinical atherosclerosis in patients with ankylosing spondylitis, even in the absence of classical dyslipidemia.

Table 23. Correlations between Framingham and SCORE2 risk scores and ultrasound parameters

Risk score	CIMT	β-stiffness	PWV	EP	ACo	AI
Framingham	rho = 0.438 (p < 0.001)	rho = 0.314 (p = 0.004)	rho = 0.326 (p = 0.003)	rho = 0.364 (p = 0.001)	rho = – 0.071 (p = 0.526)	rho = – 0.014 (p = 0.901)
SCORE2	rho = 0.488 (p < 0.001)	rho = 0.289 (p = 0.025)	rho = 0.209 (p = 0.109)	rho = 0.215 (p = 0.099)	rho = – 0.184 (p = 0.160)	rho = 0.177 (p = 0.177)

17.12 Correlations between Disease Activity, Vascular Parameters, and Markers of Endothelial Dysfunction in Patients with Psoriatic Arthritis

A detailed correlation analysis was performed in patients with psoriatic arthritis (PsA) to identify relationships among disease duration, disease activity, lipid profile, vascular–inflammatory markers, and ultrasound indices of arterial stiffness and structural vascular change.

Disease duration showed statistically significant positive correlations with all key ultrasound vascular parameters (Table 24)—carotid intima-media thickness (CIMT; rho = 0.498; p = 0.004), β-stiffness (rho = 0.467; p = 0.007), pulse wave velocity (PWV; rho = 0.485; p = 0.005), and elastic modulus (EP; rho = 0.453; p = 0.008). These findings indicate cumulative structural and functional vascular damage with longer disease course, likely reflecting a chronic systemic inflammatory process.

Table 24. Disease duration and ultrasound parameters in PsA patients

Parameter	rho (Spearman)	p-value
Duration vs CIMT	0.498	0.004
Duration vs β-stiffness	0.467	0.007
Duration vs PWV	0.485	0.005
Duration vs EP	0.453	0.008

Inflammatory activity measured by ASDAS-CRP showed a significant negative association with arterial compliance (ACo; rho = –0.275; p = 0.037), and BASDAI showed a similar negative correlation with ACo (rho = –0.298; p = 0.023). This suggests that higher disease activity—both objective and subjectively perceived—is associated with increased vascular stiffness and reduced elasticity.

Among demographic factors, age correlated strongly and positively with CIMT (rho = 0.618; p = 0.001), PWV (rho = 0.630; p < 0.001), and SCORE2 (rho = 0.765; p < 0.001), consistent with age as an established risk factor for vascular damage.

Regarding laboratory measures, in PsA patients VCAM demonstrated statistically significant positive correlations with the atherogenic index of plasma (AIP; rho = 0.456; p = 0.017) and with the overall atherogenic coefficient (rho = 0.406; p = 0.035), suggesting a potential link between endothelial dysfunction and disturbed lipid homeostasis. Conversely, VCAM correlated negatively with HDL levels (rho = –0.398; p = 0.039).

Overall, the correlation analysis indicates complex interactions among chronic inflammatory activity, lipid abnormalities, vascular stiffness, and demographic factors in PsA. The data underscore the need for early control of inflammation and metabolic abnormalities to prevent cardiovascular complications.

The aggregated findings from the study demonstrate meaningful differences among the examined groups with respect to inflammatory activity, lipid profile, ultrasound indices of arterial stiffness, and cardiovascular risk assessment. The

observed correlations between biochemical markers and vascular parameters highlight the multifactorial nature of early atherosclerotic changes in spondyloarthropathies and confirm the importance of an integrated approach to evaluating subclinical vascular injury, incorporating clinical, laboratory, and imaging parameters.

18. Regression Analysis.

18.1 Regression Analysis of Ultrasound Parameters: CIMT, β-stiffness, PWV.

To identify the independent predictors of increased carotid intima-media thickness (CIMT), a multiple linear regression analysis was conducted, including classical cardiovascular risk factors as explanatory variables. The final model incorporated age, sex, body mass index (BMI), smoking status, presence of arterial hypertension, triglycerides (TG), and LDL cholesterol as predictors. The dependent variable was CIMT.

The model demonstrated statistically significant predictive value ($F = 3.497$, $p = 0.001$), explaining 16.2% of the variation in CIMT ($R^2 = 0.162$). Among the included predictors, a statistically significant positive association with CIMT was observed for arterial hypertension ($\beta = 0.208$; $p = 0.008$) and elevated BMI ($\beta = 0.212$; $p = 0.013$). Sex also demonstrated borderline significance ($\beta = 0.144$; $p = 0.067$), with female sex being associated with higher CIMT values. Other variables (age, smoking, TG, and LDL) did not show independent statistically significant associations with CIMT in this model (Table 25).

Multicollinearity diagnostics did not reveal substantial violations—all VIF values were below 1.3. Residual diagnostics showed normally distributed errors and no autocorrelation (Durbin–Watson = 1.681), confirming the adequacy of the model. These results emphasize the leading role of arterial hypertension and excess body weight as independent contributors to early subclinical vascular wall changes.

Table 25. Multiple Linear Regression for Predictors of Carotid Intima-Media Thickness (CIMT)

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)
(Constant)	0.315	0.118	–	2.680	0.008	0.083	0.548
Sex	0.050	0.030	0.132	1.658	0.099	–0.010	0.110
Age	–0.001	0.001	–0.040	–0.495	0.621	–0.003	0.002
Hypertension	0.081	0.032	0.204	2.567	0.011	0.019	0.143
LDL	0.018	0.015	0.096	1.222	0.224	–0.011	0.048
BMI	0.006	0.003	0.174	2.196	0.030	0.001	0.012
Smoker	–0.027	0.031	–0.071	–0.897	0.371	–0.088	0.033
CRP	–0.001	0.001	–0.041	–0.523	0.602	–0.003	0.002

Following the identification of factors associated with CIMT, the next step was to determine the determinants of arterial stiffness as measured by the β-stiffness index. For this purpose, another multiple linear regression model was constructed, including the same classical cardiovascular risk factors: sex, age, arterial hypertension, TG, LDL cholesterol, BMI, and smoking.

The resulting regression function was statistically significant ($F = 3.743$, $p = 0.001$), explaining 15.2% of the variance in β-stiffness ($R^2 = 0.152$) (Table 26). The strongest predictors of increased arterial stiffness were BMI ($\beta = 0.211$; $p = 0.011$), arterial hypertension ($\beta = 0.172$; $p = 0.029$), and age ($\beta = –0.174$; $p = 0.033$). In the multivariable model, age showed a negative β-coefficient. This likely reflects collinearity with hypertension and BMI, which also increase with age, thereby "masking" the direct effect of age on β-stiffness. However, in the univariable analysis, the association was in the expected direction. Sex and lipid parameters did not reach statistical significance, although LDL showed a borderline trend ($p = 0.083$).

All VIF values were below 1.2, ruling out significant multicollinearity. Residual analysis indicated a good distribution pattern, without outliers or major deviations.

Table 26. Multiple Linear Regression for Predictors of β-stiffness

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)	VIF
(Constant)	3.940	1.739	–	2.265	0.025	0.502	7.378	–
Sex	0.751	0.445	0.132	1.686	0.094	–0.129	1.630	1.051
Age	–0.044	0.021	–0.174	–2.155	0.033	–0.085	–0.004	1.125
Hypertension	1.026	0.465	0.172	2.208	0.029	0.108	1.944	1.045
TG	–0.035	0.191	–0.015	–0.184	0.854	–0.414	0.343	1.162
LDL	0.388	0.223	0.136	1.745	0.083	–0.052	0.828	1.045
BMI	0.113	0.044	0.211	2.580	0.011	0.026	0.200	1.147
Smoker	–0.169	0.452	–0.029	–0.375	0.708	–1.063	0.724	1.055

The analysis of predictors for pulse wave velocity (PWV) demonstrated a statistically significant regression model ($F = 2.716$, $p = 0.011$) (Table 27), explaining 11.5% of the variance ($R^2 = 0.115$). Only BMI showed an independent significant association with PWV ($\beta = 0.265$; $p = 0.002$), underscoring the role of excess body weight in arterial stiffening. Other factors, including age, sex, lipid profile, hypertension, and smoking, did not show significant associations within the model. The absence of multicollinearity (VIF < 1.2) and the normal distribution of residuals confirm the adequacy of the analysis. These data highlight BMI as a key, though not exclusive, predictor of early vascular changes.

Table 27. Multiple Linear Regression for Predictors of Pulse Wave Velocity (PWV)

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)
(Constant)	4.255	0.661	–	6.434	<0.001	2.948	5.562
Sex	0.279	0.169	0.132	1.650	0.101	–0.055	0.614
Age	–0.008	0.008	–0.090	–1.085	0.280	–0.024	0.007
Hypertension	0.194	0.177	0.088	1.101	0.273	–0.155	0.544
TG	–0.010	0.073	–0.011	–0.131	0.896	–0.153	0.134
LDL	0.068	0.085	0.064	0.800	0.425	–0.100	0.235

BMI	0.053	0.017	0.265	3.181	0.002	0.020	0.086
Smoker	–0.068	0.172	–0.032	–0.394	0.694	–0.407	0.272

A multiple regression model was also examined with augmentation index (AI) as the dependent variable (Table 28), including sex, age, hypertension, smoking, TG, LDL cholesterol, and BMI. The model was statistically significant ($F = 3.070$, $p = 0.005$), suggesting an association between some predictors and arterial wave reflection. Among all included variables, only sex showed an independent association with AI ($\beta = 0.256$, $p = 0.002$), with female sex linked to higher index values. LDL cholesterol showed borderline significance ($\beta = 0.167$, $p = 0.036$), whereas age, hypertension, smoking, TG, and BMI were not significant predictors ($p > 0.05$). Smoking was not associated with changes in the dependent variable ($\beta \approx 0$, $p = 1.000$), suggesting a lack of independent effect within the studied cohort. The absence of effect of smoking is likely due to the limited statistical power and the relatively small number of active smokers in the cohort. In addition, smoking may interact with other factors (lipid profile, inflammation, hypertension), which could mask its direct association with vascular parameters. The literature provides unequivocal evidence of its detrimental impact on vascular function; therefore, the present finding should be interpreted with caution. No serious issues with multicollinearity were identified (all VIF < 1.2), and residual diagnostics indicated normality and homoscedasticity.

Table 28. Multiple Linear Regression for Predictors of Augmentation Index (AI)

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)
(Constant)	4.036	9.304	–	0.434	0.665	–14.351	22.423
Sex	7.679	2.381	0.256	3.226	0.002	2.974	12.384
Age	0.019	0.110	0.014	0.171	0.864	–0.198	0.236
Hypertension	3.853	2.485	0.122	1.551	0.123	–1.058	8.764
Smoker	–0.00007	2.418	0.000	0.000	1.000	–4.779	4.779
TG	–1.088	1.024	–0.088	–1.063	0.290	–3.112	0.936
LDL	2.521	1.190	0.167	2.118	0.036	0.168	4.874

BMI	–0.245	0.234	–0.086	–1.045	0.298	–0.708	0.218

The multiple linear regression including predictors (sex, age, hypertension, smoking, TG, LDL, and BMI) (Table 29) did not show a statistically significant model ($F = 1.317$; $p = 0.246$), with low explanatory power ($R^2 = 0.059$; adjusted $R^2 = 0.014$). None of the independent variables reached statistical significance at $p < 0.05$. The closest to significance were BMI ($B = –0.011$; $p = 0.412$), LDL ($B = 0.088$; $p = 0.210$), and hypertension ($B = 0.216$; $p = 0.143$). This suggests that in the current model neither anthropometric, lipid, nor demographic variables provided an independent predictive contribution to the variation in ACo. The absence of significant independent predictors in this model likely reflects the limited statistical power, as well as the presence of interactions between classical risk factors. The negative signs for BMI and smoking should be considered statistical artifacts, as they contradict established pathophysiological mechanisms. In our other models, BMI and LDL demonstrated stronger and statistically significant effects, suggesting that the choice of dependent variable and the structure of the sample exert a substantial influence on the final outcome.

Table 29. Multiple Linear Regression – Dependent Variable ACo

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)
Sex	–0.234	0.140	–0.137	–1.666	0.098	–0.512	0.044
Age	0.009	0.006	0.122	1.435	0.154	–0.004	0.022
Hypertension	0.216	0.147	0.121	1.474	0.143	–0.074	0.506
Smoker	–0.180	0.143	–0.104	–1.261	0.209	–0.462	0.102
TG	0.019	0.060	0.027	0.316	0.753	–0.100	0.138
LDL	0.088	0.070	0.103	1.258	0.210	–0.050	0.227
BMI	–0.011	0.014	–0.071	–0.823	0.412	–0.039	0.016

In the subsequent multiple linear regression model, with EP as the dependent variable, the same seven predictors were included (Table 23). The model demonstrated

statistical significance ($p < 0.001$) and explained 15.9% of the variance in EP ($R^2 = 0.159$), with an adjusted R^2 of 0.119. This indicates a moderate predictive value of the included variables. Among all predictors, only BMI showed an independent statistically significant association with EP ($\beta = 0.281$; $p < 0.001$), suggesting that higher body weight is associated with a significant increase in the elastic modulus of the arterial wall. The other predictors – sex, age, hypertension, smoking, LDL, and TG – did not reach statistical significance, although hypertension demonstrated borderline relevance ($p = 0.053$). No serious problems with multicollinearity were observed, as confirmed by VIF values (<1.2) and collinearity diagnostics.

18.2 Regression Analysis of Adhesion Molecules

In an effort to identify independent predictors associated with serum levels of vascular cell adhesion molecule-1 (VCAM-1), a multiple linear regression analysis was performed (Table 30), including classical cardiovascular risk factors and selected ultrasound parameters of arterial stiffness. The model incorporated age, sex, body mass index (BMI), presence of arterial hypertension, smoking status, LDL-cholesterol levels, CRP, and the β-stiffness index. The dependent variable was VCAM.

The regression model demonstrated borderline statistical significance ($F = 1.986$, $p = 0.052$), explaining 9.9% of the variance ($R^2 = 0.099$). Among the included predictors, BMI showed a statistically significant positive association with VCAM levels ($\beta = 0.185$; $p = 0.026$), while CRP values demonstrated a trend toward significance ($\beta = 0.147$; $p = 0.067$). The remaining variables—including age, sex, arterial hypertension, β-stiffness, and LDL—did not reach statistical significance in this model. Multicollinearity diagnostics revealed no substantial violations (all VIF < 1.2), and the Durbin–Watson statistic (1.982) confirmed the absence of autocorrelation. Residual analysis supported the adequacy of the model. The results are presented in Table 30.

Table 30. Multiple Linear Regression for Predictors of VCAM

Predictor	B (Unstd.)	Std. Error	β (Std.)	t	p-value	95% CI (Lower)	95% CI (Upper)
(Constant)	361.824	187.611	–	1.929	0.056	–8.982	732.630
Sex	45.335	47.605	0.078	0.952	0.343	–48.755	139.424
Age	3.180	2.160	0.122	1.472	0.143	–1.089	7.449
Hypertension	27.060	50.280	0.044	0.538	0.591	–72.316	126.436
LDL	–30.912	23.721	–0.106	–1.303	0.195	–77.795	15.970
BMI	10.150	4.523	0.185	2.244	0.026	1.211	19.089
Smoker	–5.696	47.892	–0.010	–0.119	0.905	–100.353	88.961
β-stiffness	7.673	8.794	0.075	0.873	0.384	–9.708	25.055
CRP	3.326	1.806	0.147	1.842	0.067	–0.243	6.895

IV. DISCUSSION

1. Demographic and Clinical Characteristics

The present study identified substantial differences in the demographic profiles of the three groups examined—patients with ankylosing spondylitis (AS), psoriatic arthritis (PsA), and healthy controls. The sex distribution in AS revealed a predominance of men (66.3%), whereas in PsA women were the majority (67.5%). This trend is consistent with the epidemiological characteristics of the two diseases: AS is more common in men, with a male-to-female ratio of 2–3:1 (Gran et al., 1985), whereas PsA shows no clearly established sex predisposition (Gelfand et al., 2005; Stolwijk et al., 2016).

With respect to age, PsA patients were significantly older (mean age 54.03 ± 11.01 years) compared to AS patients (47.05 ± 10.62 years) and the control group (48.35 ± 11.27 years) ($p = 0.004$). This corresponds to the later clinical manifestation of PsA described in the literature (Ogdie et al., 2015). The observed age difference is important when interpreting cardiovascular risk, as age is an independent determinant in most risk scores.

The body mass index (BMI) did not differ significantly between groups ($p = 0.630$), although the highest values were recorded in PsA (28.47 ± 5.64 kg/m²), followed by AS (27.75 ± 5.31 kg/m²) and controls (26.73 ± 4.78 kg/m²). This trend reflects the greater prevalence of overweight and metabolic disturbances in PsA, as highlighted in the literature review (Stolwijk et al., 2016).

Smoking was common across all groups—65.0% in PsA, 55.4% in AS, and 64.5% in controls—with no statistically significant difference ($p = 0.497$). Although not directly discussed in the review, the high prevalence of smoking is relevant to the interpretation of vascular indices and contributes to overall cardiovascular risk.

The prevalence of arterial hypertension was highest in PsA patients (47.5%), compared to 27.7% in AS and 35.5% in controls. Although these differences did not reach statistical significance ($p = 0.095$), the findings reinforce the higher metabolic burden in PsA, consistent with evidence of increased cardiovascular and metabolic risk in this population (Stolwijk et al., 2016). In AS, the lower frequency of hypertension may be explained by a different inflammatory profile and less pronounced metabolic comorbidity (Braun et al., 1998).

The heterogeneity in sex and age between patients with AS and PsA reflects the epidemiological characteristics of the two diseases, but it may influence vascular parameters. In addition, differences in disease duration and the delay between symptom onset, diagnosis, and initiation of therapy are typical in clinical practice and may also have an impact on vascular changes.

In summary, the demographic and clinical characteristics of the participants confirm the well-established differences between AS and PsA. PsA patients are characterized by older age, higher BMI, and a greater prevalence of arterial hypertension—all factors that may contribute to increased cardiovascular risk and

2. Disease Activity

The analysis of disease activity indices showed that most patients with ankylosing spondylitis and psoriatic arthritis had low to moderate clinical activity at the time of

enrollment. In AS, the mean ASDAS-CRP was 2.30 ± 1.30, with a wide range of values (1.13–6.90), indicating the presence of both patients with low activity and those with high activity. The mean BASDAI was 2.83 ± 1.96, further confirming the predominantly low to moderate inflammatory burden in this group.

In PsA, disease activity was assessed using DAS28, with values ranging from 2.06 to 5.89 and a mean of 2.82 ± 0.83. The distribution indicated that most participants fell within the ranges of low to moderate activity, with only a limited number of patients presenting high values. These findings suggest that disease activity was partially controlled in the majority of the studied population, despite variability in therapeutic approaches and individual characteristics.

3. Lipid Profile and Atherogenic Indices

In the present study, no statistically significant differences were observed in the main lipid parameters between patients with ankylosing spondylitis (AS), psoriatic arthritis (PsA), and the control group. Nevertheless, certain trends were noted, suggesting a moderately atherogenic metabolic profile in patients. The mean HDL-cholesterol levels were 1.49 ± 0.39 mmol/L in PsA, 1.44 ± 0.41 mmol/L in AS, and 1.54 ± 0.44 mmol/L in controls, without significant differences. Similar moderate reductions in HDL associated with chronic inflammation have been reported in previous studies.

According to Kucuk et al. (2017), HDL was significantly reduced in PsA compared to controls (1.09 ± 0.4 vs. 1.44 ± 0.4 mmol/L), highlighting the less favorable metabolic profile in certain cohorts. Cure et al. (2018) also reported decreased HDL-C and increased Castelli I index in PsA patients. In our study, the Castelli I index was highest in AS (3.95 ± 1.13), followed by PsA (3.77 ± 1.06) and controls (3.58 ± 0.83), indicating a slightly elevated atherogenic risk despite preserved absolute lipid values.

Divecha et al. (2005) found reduced HDL levels in AS, even in patients with low clinical activity. Mathieu et al. (2010) reported that anti-TNF therapy increased HDL levels, but without substantial improvement in atherogenic ratios—a finding consistent

with our observations, where no significant HDL differences were detected between treated and untreated patients.

Van Halm et al. (2006) observed lower LDL and significantly reduced HDL in AS compared to controls (1.17 ± 0.36 mmol/L vs. 1.34 ± 0.35 mmol/L), consistent with our findings. Van Eijk et al. (2009) also confirmed unfavorable atherogenic ratios in AS, regardless of therapy. Ceccon et al. (2013) similarly reported significantly reduced HDL in PsA, emphasizing the role of inflammation in this alteration.

In our cohort, the mean AIP index was –0.061 ± 0.318 in AS and –0.045 ± 0.289 in PsA, corresponding to a low-to-moderate cardiovascular risk. The Castelli II index values (2.38 ± 0.88 in AS; 2.20 ± 0.78 in PsA; 2.08 ± 0.60 in controls) and the atherogenic coefficient (2.36 ± 1.13 in AS; 2.32 ± 1.15 in PsA; 2.13 ± 0.79 in controls) also indicated a moderately increased atherogenic profile in both diseases.

In summary, our data support the concept that even in the absence of significant alterations in standard lipid parameters, patients with spondyloarthritis exhibit elevated atherogenic ratios, likely reflecting inflammation-mediated changes in lipoprotein profiles. These findings are clinically relevant, as such imbalances may contribute to an increased risk of subclinical atherosclerosis and cardiovascular events.

4. Applicability of Traditional Cardiovascular Risk Scores in Inflammatory Joint Diseases

The assessment of cardiovascular risk using the Framingham and SCORE2 models in our cohort revealed different discriminatory capacities between the two scores. According to the Framingham score, mean values were comparable across groups (AS: 5.43 ± 4.91%; PsA: 5.27 ± 4.34%; controls: 6.76 ± 4.48%), with no convincing intergroup differences. This aligns with evidence that Framingham often underestimates risk in chronic inflammatory diseases and demonstrates reduced sensitivity in such populations (Wright et al., 2015; Heslinga et al., 2015).

By contrast, SCORE2 revealed clearer trends, with the highest mean risk observed in PsA (11.52 ± 7.69%), followed by controls (8.89 ± 6.24%) and AS (8.61 ± 6.72%).

The higher SCORE2 values in PsA are consistent with the greater metabolic burden (higher BMI, more frequent hypertension/dyslipidemia) and the synergistic impact of inflammation with traditional risk factors (Heslinga et al., 2015). The minimal difference between AS and controls likely reflects the age structure and unfavorable risk profile of certain control participants (e.g., higher prevalence of smoking/hypertension), which elevates baseline risk and reduces the case–control contrast.

Our findings are in line with comparative analyses showing superior discrimination of SCORE2-based models compared to Framingham in SpA, emphasizing the importance of incorporating inflammatory markers (CRP) in risk assessment (Navarini et al., 2020). Additionally, studies in PsA demonstrate that applying the EULAR correction factor (1.5 multiplier) increases the proportion of patients classified as high/very high risk (Degboé et al., 2022), supporting the view that standard calculators systematically underestimate risk.

In our cohort, vascular ultrasound parameters (CIMT, β-stiffness, PWV, EP) correlated positively with SCORE2 and Framingham, while arterial compliance (ACo) correlated negatively, which is physiologically consistent and strengthens the validity of these associations. This pattern aligns with evidence that imaging markers capture early subclinical vascular changes even when risk scores remain low to moderate (Rueda-Gotor et al., 2016).

In summary, among our patients, SCORE2 demonstrated greater sensitivity to group differences, particularly in PsA, whereas Framingham yielded comparable values across groups. Combining SCORE2 with ultrasound vascular markers and inflammatory parameters provides a more comprehensive assessment of true cardiovascular risk and mitigates the underestimation inherent in traditional scores (Wright et al., 2015; Heslinga et al., 2015; Navarini et al., 2020; Degboé et al., 2022; Rueda-Gotor et al., 2016).

5. Adhesion Molecules (ICAM-1, VCAM-1): Own Results and Comparison with the Literature

In our cohort, no statistically significant intergroup differences were observed in ICAM-1 and VCAM-1 levels between patients with AS, PsA, and healthy controls (ICAM-1: $H = 1.902$, $p = 0.386$; VCAM-1: $H = 4.665$, $p = 0.097$). Mean VCAM-1 levels were highest in PsA (927.15 ng/mL), followed by controls (852.10 ng/mL) and AS (813.94 ng/mL), though these differences did not reach statistical significance. This contrasts with published data. Wendling et al. (1998) investigated serum sICAM-1 levels in patients with spondyloarthritis and found significantly higher values compared with controls, correlating with ESR and CRP; endothelial dysfunction was not directly measured but inferred from serum markers. Liu et al. (2016) reported elevated ICAM-1 and VCAM-1 in AS, associated with disease activity, using flow cytometry for adhesion molecules and flow-mediated dilation (FMD) to assess endothelial function, demonstrating an inverse correlation between FMD and adhesion molecule levels. Frers et al. (2018) analyzed early PsA patients without classical cardiovascular risk factors and showed that ICAM-1 and VCAM-1 were increased and positively correlated with CIMT, assessed by high-frequency B-mode ultrasound. Gündüz et al. (2023) observed higher VCAM-1 levels in PsA, associated with endothelial dysfunction measured by FMD and arterial stiffness (PWV). Garg et al. (2015) and Ibrahim et al. (2014) also described elevated ICAM-1 and VCAM-1 in PsA, linking them to CIMT and FMD as markers of subclinical atherosclerosis and endothelial dysfunction.

The discrepancy with our results may be explained by the lower mean disease activity in our cohort, the high proportion of patients receiving biologic therapy, and the relatively smaller subgroup sizes. Additionally, some of the cited studies excluded patients on immunosuppressive treatment, which could have resulted in higher adhesion molecule levels.

Despite the absence of intergroup differences, within-group analysis revealed that VCAM-1 was significantly higher in AS patients with greater disease activity

(ASDAS-CRP stratification; p = 0.002). This finding is consistent with Schmieder et al. (2007), who demonstrated that inflammatory cytokines stimulate endothelial VCAM-1 expression. Similar correlations between VCAM-1 and inflammatory markers (CRP, ESR) were reported by Liu et al. (2016) and Wendling et al. (1998).

In our study, VCAM-1 didn't correlate with lipid parameters. Khovidhunkit et al. (2004) described mechanisms whereby inflammation induces HDL dysfunction and pro-atherogenic alterations in lipid metabolism, while Feingold et al. (2022) emphasized that chronic inflammation disrupts reverse cholesterol transport. Garg et al. (2015) further demonstrated that PsA patients with elevated adhesion molecules also exhibited higher atherogenic indices.

With respect to therapeutic subgroups, our cohort showed lower VCAM-1 levels in patients receiving JAK inhibitors compared with biologic-naïve patients (p = 0.014), and in those on anti-TNF therapy (p = 0.046). Genre et al. (2017) reported that infliximab treatment in AS improved endothelial function measured by FMD and reduced endothelial activation markers. Garg et al. (2015; 2021) also described reductions in VCAM-1 and improvements in vascular function following anti-inflammatory therapy. Although clinical data on JAK inhibitors in SpA remain limited, in vitro studies have shown suppression of endothelial VCAM-1 expression. In contrast, Sari et al. (2010) found no significant differences in adhesion molecule levels between patients on different therapies, suggesting that the differences observed in our study may reflect the specific sample characteristics and predominance of patients with low disease activity.

In our cohort, ICAM-1 did not show significant intergroup differences and no consistent associations with major clinical or vascular parameters. Azevedo et al. (2013) reported associations between ICAM-1 and hypertension, dyslipidemia, and smoking in AS. Wendling et al. (1998) and Liu et al. (2016) described correlations of ICAM-1 with CRP and ESR. Frers et al. (2018), Garg et al. (2015), and Ibrahim et al. (2014) linked ICAM-1 to increased CIMT and subclinical atherosclerosis in PsA, with CIMT assessed by B-mode ultrasound.

6. Ultrasound Vascular Markers: Comparative Analysis and Interpretation

Carotid intima–media thickness (CIMT) is a well-established noninvasive marker of early atherosclerotic change and a predictor of future cardiovascular events (Lorenz et al., 2007). In the present study, mean CIMT values were highest in patients with psoriatic arthritis (0.638 mm), followed by those with ankylosing spondylitis (0.598 mm) and the control group (0.518 mm). Intergroup analysis revealed a statistically significant difference ($p = 0.013$). Pairwise comparisons demonstrated higher CIMT in PsA compared with controls ($p = 0.002$), borderline significance in AS compared with controls ($p = 0.062$), and no significant difference between AS and PsA ($p = 0.152$). These results are consistent with the literature showing accelerated development of subclinical atherosclerosis in inflammatory arthropathies, particularly in PsA (Eder et al., 2015; Gonzalez-Juanatey et al., 2007).

Correlation analysis in our cohort demonstrated moderate-to-strong positive associations between CIMT and local functional indices of arterial stiffness – PWV ($r = 0.528$; $p < 0.001$), β-stiffness ($r = 0.500$; $p < 0.001$), and EP ($r = 0.520$; $p < 0.001$) – as well as a weaker but significant correlation with AI ($r \approx 0.21$; $p \approx 0.01$). Regarding global cardiovascular risk scores, a weak but statistically significant positive correlation was observed between CIMT and SCORE2 ($r = 0.239$; $p = 0.003$). Framingham, however, did not show significant associations with CIMT or other stiffness parameters ($p > 0.05$).

Among classical risk factors, CIMT correlated positively with age and hypertension. In multivariable regression analysis, BMI emerged as an independent predictor of increased CIMT ($p = 0.030$). This suggests that in well-treated patients, structural vascular changes are determined primarily by cumulative hemodynamic and metabolic factors rather than current inflammatory activity, which aligns with other studies (Gonzalez-Juanatey et al., 2008; Mathieu et al., 2011). The absence of association with CRP and ESR in our cohort likely reflects the impact of targeted therapies and adequate disease control, similar to reports of slowed atherosclerotic

progression in patients receiving anti-TNF treatment (Ji et al., 2025; Di Minno et al., 2012; Ortolan et al.).

In summary, CIMT in our study is a sensitive marker of structural vascular involvement in AS and PsA, closely linked to local indices of arterial stiffness and, to a lesser extent, to SCORE2, but not to Framingham. Higher values in PsA and associations with BMI and hypertension underscore the importance of early cardiovascular surveillance, particularly in the presence of metabolic comorbidities.

Extending the analysis of vascular parameters, the β-stiffness index, reflecting arterial rigidity, also showed significant intergroup differences ($p < 0.001$). The highest values were observed in PsA patients (8.85 ± 3.76), followed by AS (7.36 ± 2.40), with controls demonstrating significantly lower values (5.76 ± 1.20). Pairwise comparisons confirmed significantly higher stiffness in both inflammatory arthropathy groups compared with controls ($p < 0.001$), consistent with the more pronounced CIMT changes. The lack of a statistically significant difference between AS and PsA ($p = 0.105$) suggests shared pathogenic mechanisms—chronic systemic inflammation, oxidative stress, and vascular wall remodeling—leading to reduced elasticity of large arteries (Laurent et al., 2006; Zieman et al., 2005). The trend toward higher β-stiffness in PsA may be linked to greater vascular involvement described in the disease, including more pronounced dyslipidemia, metabolic abnormalities, and higher prevalence of cardiometabolic risk factors that amplify the vascular impact of inflammation (Yasmin et al., 2005). These findings highlight β-stiffness as a reliable marker of early vascular impairment in inflammatory arthropathies, even in the absence of overt atherosclerosis.

In line with the β-stiffness results, pulse wave velocity (PWV) – the gold standard for assessing arterial stiffness – also demonstrated significant intergroup differences ($p = 0.001$). PWV was significantly higher in patients with AS and PsA compared with controls, with no significant difference between the two disease groups. Absolute values in our cohort (AS: 5.99 m/s; PsA: 6.33 m/s; controls: 5.32 m/s) were lower than those reported in some studies, such as Costa et al. (2012), who found significantly

increased PWV in PsA compared with controls (8.3 ± 0.2 vs. 6.8 ± 0.2 m/s; $p < 0.0001$). These discrepancies may reflect younger mean age, lower hypertension prevalence, and the widespread use of biologic therapy in our sample, which may improve vascular function. Similar to our results, Shen et al. (2015) observed associations between elevated PWV and cumulative inflammatory activity in PsA, supporting the role of chronic inflammation in arterial remodeling. Ullensvang et al. (2023) reported that in AS, hypertension was associated with a fourfold increased risk of cardiovascular organ damage, including elevated PWV, underscoring the contribution of comorbid cardiovascular risk factors. In summary, our findings are consistent with the literature, confirming that PWV is elevated in AS and PsA, with inflammation and hypertension being key drivers of this process, while optimal disease and risk factor control may contribute to lower values.

Beyond PWV, other ultrasound parameters – arterial compliance (ACo), augmentation index (AI), and elastic modulus (EP) – also revealed significant intergroup differences and specific associations with vascular damage and cardiovascular risk. Arterial compliance showed clear and statistically significant differences between groups ($p < 0.001$), with the lowest values in PsA (15.91 ± 4.56 mm^2/kPa), followed by AS (16.83 ± 5.12 mm^2/kPa), while controls had markedly higher values (20.42 ± 4.17 mm^2/kPa). Reduced arterial compliance was associated with an unfavorable lipid profile—negative correlations with LDL ($r = –0.258$, $p = 0.002$), the atherogenic coefficient ($r = –0.311$, $p < 0.001$), and AIP ($r = –0.296$, $p < 0.001$), and a positive correlation with HDL ($r = 0.298$, $p < 0.001$).

The augmentation index showed significant intergroup differences ($p = 0.002$), with the highest values in PsA (18.32 ± 7.05%), followed by AS (16.74 ± 6.42%), and the lowest in controls (12.84 ± 5.37%). Elevated AI correlated positively with CIMT ($r = 0.272$, $p < 0.001$), β-stiffness ($r = 0.512$, $p < 0.001$), PWV ($r = 0.521$, $p < 0.001$), and SCORE2 ($r = 0.268$, $p < 0.001$), suggesting that increased wave reflection and peripheral vascular tone are closely linked to advanced vascular remodeling and higher estimated 10-year risk of fatal cardiovascular events.

The elastic modulus, reflecting arterial wall stiffness, reached the highest values in PsA (476.2 ± 113.7 kPa), followed by AS (452.5 ± 105.6 kPa), and was lowest in controls (395.4 ± 98.2 kPa), with statistically significant differences ($p = 0.045$). EP correlated positively with CIMT ($r = 0.262$, $p = 0.001$), β-stiffness ($r = 0.508$, $p < 0.001$), PWV ($r = 0.498$, $p < 0.001$), and SCORE2 ($r = 0.237$, $p = 0.003$), confirming the link between increased arterial rigidity, structural vascular changes, and elevated cardiovascular risk.

V. CONCLUSIONS

1. Patients with ankylosing spondylitis and psoriatic arthritis exhibit ultrasound evidence of subclinical atherosclerosis, expressed by increased CIMT, β-stiffness, PWV, and EP values compared to controls, with psoriatic arthritis showing a tendency toward more pronounced vascular changes.
2. Significant associations were found between arterial stiffness and traditional cardiovascular risk factors such as age and hypertension, in the absence of statistically significant differences between the groups in Framingham and SCORE2 risk scores. This highlights the limited sensitivity of traditional models for detecting subclinical vascular damage in inflammatory diseases.
3. The relationship between disease activity and vascular parameters differs between the two diseases, suggesting distinct patterns of vascular involvement – predominantly inflammatory in ankylosing spondylitis and more complex, influenced by traditional risk factors, in psoriatic arthritis.
4. VCAM-1 emerges as a sensitive serum marker of endothelial dysfunction and a potential indicator of early vascular impairment in patients with spondyloarthritis.
5. Although lipid fractions and atherogenic indices do not differ significantly between disease groups, their correlation with vascular parameters supports the role of combined metabolic and inflammatory influences on the arterial wall.

6. Biological and targeted synthetic therapies exert differential effects on vascular and inflammatory markers – JAK inhibitors are associated with lower VCAM-1 levels, whereas anti-TNF therapy corresponds to higher CRP, triglycerides, and AIP values, suggesting distinct vascular and metabolic profiles among therapeutic classes.

VI. CONTRIBUTIONS

1. **Scientific and theoretical contributions**

- For the first time in Bulgaria, both structural (CIMT) and functional (β-stiffness, PWV, AI, ACo, EP) indices of arterial stiffness were simultaneously investigated in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA), assessed by echo-tracking methodology, in combination with evaluation of endothelial activation markers ICAM-1 and VCAM-1.
- This is the first national study to compare the effects of different targeted therapies (anti-TNF, anti-IL-17, JAK inhibitors) on endothelial function and arterial elasticity in patients with spondyloarthropathies.

2. **Scientific and practical contributions**

- It was confirmed that the echo-tracking technique is a valuable non-invasive tool for detecting subclinical atherosclerosis in patients with inflammatory arthropathies, suitable for implementation in routine clinical practice.
- The importance of an integrated assessment—including vascular indices, lipid profile, and inflammatory status—was emphasized for the individualized evaluation of cardiovascular risk in AS and PsA patients.
- Potentially beneficial effects of JAK inhibitors on VCAM-1 levels and arterial elasticity were identified, which may have implications for therapeutic decision-making.

- Associations were outlined between lipid profile components (total cholesterol, triglycerides, HDL) and indices of arterial stiffness, with practical relevance for monitoring and preventing cardiovascular complications.

3. **Confirmatory contributions**
   - The significant contribution of triglycerides and total cholesterol to intima-media thickening in patients with inflammatory arthropathies was confirmed.
   - Increased arterial stiffness in AS and PsA patients compared with healthy controls, measured by ultrasound methods, was confirmed.
   - Arterial hypertension was confirmed to be associated with more pronounced structural and functional vascular alterations (higher CIMT, β-stiffness, AI, EP) and with elevated cardiovascular risk scores.

VII. LIMITATIONS OF THE STUDY

1. **Study design** – The study employed a cross-sectional design, which does not allow for causal inferences between inflammatory activity, lipid metabolism, endothelial function, and indices of arterial stiffness.
2. **Sample size and subgroups** – Although the total number of participants was relatively large for a single-center study (n = 154), the size of certain subgroups (e.g., patients on JAK inhibitors, biologic-naïve, or with high disease activity) was small, limiting statistical power and increasing the risk of type II error.
3. **Lack of follow-up** – Data were based on a single time-point assessment and do not capture the longitudinal dynamics of the parameters or their changes after therapy adjustment. Consequently, the long-term effects of treatment could not be evaluated.

4. **Therapeutic heterogeneity** – Patients were receiving different targeted therapies of varying duration. No stratification by treatment exposure time was performed, which may have influenced lipid and vascular profiles.
5. **Conducting pairwise comparisons** in the absence of overall significance from the Kruskal–Wallis test represents an exploratory approach and increases the risk of type I error. However, this was performed in order to provide a more detailed characterization of the therapeutic subgroups under the conditions of a limited sample size.
6. **Potential confounding factors** – Full adjustment for possible confounders such as dietary habits, physical activity, comorbidities, and concomitant medications was not applied.
7. **Methodological aspects** – Vascular measurements (CIMT, PWV, β-stiffness, AI, ACo, EP) were performed with a single device and operator. While this reduces inter-operator variability, it does not allow assessment of reproducibility across different examiners or equipment.
8. **The heterogeneity in sex and age** between patients with AS and PsA reflects the epidemiological characteristics of the two diseases, but it may influence vascular parameters. Furthermore, differences in disease duration and the delay between symptom onset, diagnosis, and initiation of therapy are typical in clinical practice and may also affect vascular changes.

VIII. CONCLUSION

The results of this study demonstrate that patients with ankylosing spondylitis and psoriatic arthritis, even in the absence of overt cardiovascular symptoms, exhibit significant structural and functional alterations of the arterial wall, consistent with subclinical atherosclerosis and increased arterial stiffness. Changes in indices measured by high-sensitivity echo-tracking (CIMT, β-stiffness, PWV, AI, ACo, EP) correlated with age and the presence of arterial hypertension, as well as with

unfavorable alterations in lipid profile and atherogenic indices. Endothelial activation markers, particularly VCAM-1, also showed meaningful associations with vascular stiffness parameters and lipid metabolism, underscoring its potential role as an early biomarker of vascular injury in inflammatory arthropathies.

The observed associations between vascular indices, lipid profile, and inflammatory markers confirm the multifactorial nature of the atherosclerotic process in the context of chronic systemic inflammation. These findings emphasize the need for a comprehensive cardiovascular risk assessment in this population, one that incorporates not only traditional risk factors but also disease-specific parameters. Despite the heterogeneity of therapeutic regimens, the data suggest a potentially favorable influence of certain targeted therapies on vascular status, opening perspectives for personalized treatment strategies.

In conclusion, the integration of ultrasound-based assessment of arterial stiffness and intima–media thickness, combined with measurement of adhesion molecules and atherogenic indices, provides valuable insights for the early detection of vascular pathology in patients with ankylosing spondylitis and psoriatic arthritis. Such an approach enables timely risk stratification and preventive measures against major cardiovascular events, thereby contributing to improved long-term prognosis and quality of life in these patients.

IX. List of Publications and Conference Contributions Related to the Dissertation

- Angelov, A.K., Markov, M., Ivanova, M. et al. *The genesis of cardiovascular risk in inflammatory arthritis: insights into glycocalyx shedding, endothelial dysfunction, and atherosclerosis initiation.* Clin Rheumatol 42, 2541–2555 (2023). https://doi.org/10.1007/s10067-023-06738-x
- Markov, M., Georgiev, T., Angelov, A.K. et al. *Adhesion molecules and atherosclerosis in ankylosing spondylitis: implications for cardiovascular risk.*

Rheumatol Int 44, 1837–1848 (2024). https://doi.org/10.1007/s00296-024-05693-3

Conference Presentations

- Presentation at the IV Scientific Conference *"Residual Cardiovascular Risk and Control of Global Risk: Why Does the Risk Persist?"*, February 2–3, 2024.
- Presentation at the National Rheumatology Conference, Pravets, September 28 – October 1, 2023.

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