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Left atrium and right ventricle strain in rheumatoid arthritis patients with preserved left ventricle systolic function

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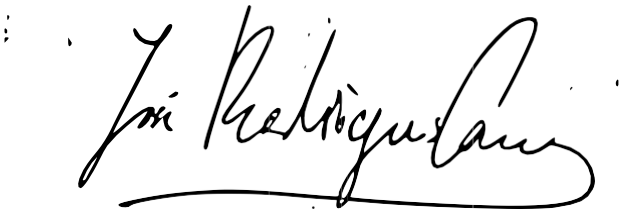
ASSINATURAS

Assinatura do Estudante



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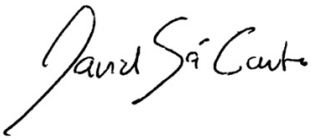

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As avós, que partiram cedo demais, Lí e Lú.

Ao avô e eterno professor, Manuel.

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RESUMO

Introdução: A artrite reumatoide (AR) é uma doença inflamatória crónica associada a um aumento da morbilidade e mortalidade cardiovasculares, mesmo na ausência de doença cardíaca evidente. A disfunção miocárdica subclínica pode preceder insuficiência cardíaca com manifestações clínicas em doentes com função sistólica preservada do ventrículo esquerdo (VE). Técnicas ecocardiográficas avançadas, como a ecocardiografia com *speckle-tracking*, podem permitir a deteção precoce de disfunção cardíaca através da análise da deformação miocárdica.

Objetivos: Este estudo teve como objetivo caracterizar o *strain* (deformação) da aurícula esquerda (AE) e do ventrículo direito (VD) em doentes com AR sem doença cardíaca conhecida e com função sistólica do VE preservada, bem como investigar a sua associação com características clínicas, atividade da doença e eventos cardiovasculares.

Métodos: Foi realizada uma análise retrospetiva, unicêntrica, de uma coorte prospetiva de doentes com AR avaliados entre 2016 e 2018. Foram excluídos doentes com doença cardiovascular prévia, disfunção sistólica do VE ou qualidade de imagem inadequada. O *strain* da AE e do VD foi avaliado através de ecocardiografia com recurso a *speckle-tracking*. Os doentes foram categorizados de acordo com os valores normais ou reduzidos de *strain*, com base em valores de referência estabelecidos. Foram analisados dados clínicos, laboratoriais e ecocardiográficos, e os doentes foram seguidos até 7 anos para eventos cardiovasculares adversos (ACE), incluindo a morte de causa cardiovascular, hospitalização por insuficiência cardíaca, fibrilhação auricular, enfarte do miocárdio e acidente vascular cerebral.

Resultados: Foram incluídos 260 doentes (idade média de 56 anos, 80,4% do sexo feminino) na análise da *strain* da AE, e 180 na análise da *strain* do VD. Foi observada redução do *strain* da AE em 8,5% dos doentes, associada a idade mais avançada, menor capacidade funcional, maior atividade da doença, concentrações superiores de NT-proBNP e marcadores de disfunção diastólica, incluindo um rácio E/e' mais elevado. A redução do *strain* do VD esteve presente em 18,9% dos doentes e associou-se a uma maior prevalência de fatores de risco cardiovascular tradicionais, incluindo tabagismo, frequência cardíaca e pressão arterial diastólica mais elevadas e perfil lipídico mais adverso, mas não foi demonstrada relação com marcadores inflamatórios ou de atividade da doença. Durante o seguimento, a incidência de ACE foi baixa, não tendo a redução da *strain* da AE nem do VD demonstrado associação estatisticamente significativa com os eventos adversos. No entanto, ambos os parâmetros de *strain* apresentaram correlações

significativas com anomalias da estrutura e função cardíaca, incluindo o *strain* longitudinal global do VE.

Conclusão: Em doentes com AR sem doença cardiovascular evidente e com função sistólica do VE preservada, a maioria apresenta valores normais de *strain* da AE e do VD. A redução do *strain* da AE associa-se a uma menor capacidade funcional e elevação de marcadores laboratoriais de disfunção cardíaca e de atividade da doença inflamatória, enquanto a redução do *strain* do VD parece estar mais relacionado com fatores de risco cardiovascular tradicionais. Apesar de não ter sido demonstrado um valor prognóstico de forma independente, a imagiologia de deformação miocárdica pode fornecer informação relevante sobre o envolvimento cardíaco subclínico na AR e contribuir para uma melhor estratificação de risco nesta população.

ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with increased cardiovascular morbidity and mortality, even in the absence of overt cardiac disease. Subclinical myocardial dysfunction may precede clinically evident heart failure (HF) in patients with preserved left ventricular (LV) systolic function. Advanced echocardiographic techniques, such as speckle-tracking echocardiography, may enable early detection of subtle cardiac abnormalities through myocardial deformation analysis.

Objectives: This study aimed to characterize left atrial (LA) and right ventricular (RV) strain in patients with RA without known cardiovascular disease and preserved LV systolic function, and to investigate their association with clinical characteristics, biomarkers of disease activity, and cardiovascular outcomes.

Methods: This was a single-center retrospective analysis of a prospectively enrolled cohort of RA patients evaluated between 2016 and 2018. Patients with prior cardiovascular disease, LV systolic dysfunction, or inadequate imaging quality were excluded. LA and RV strain were assessed using vendor-independent speckle-tracking echocardiography. Patients were categorized according to normal or reduced strain values based on established reference thresholds. Clinical, laboratory, and echocardiographic data were analyzed, and patients were followed for up to 7 years for adverse cardiovascular events (ACE), defined as a composite of cardiovascular death, HF hospitalization, atrial fibrillation, myocardial infarction, and stroke.

Results: A total of 260 patients (mean age 56 years, 80.4% female) were included for LA strain analysis, and 180 for RV strain analysis. Reduced LA strain was observed in 8.5% of patients and was associated with older age, reduced functional capacity, higher disease activity (DAS28-ESR), elevated NT-proBNP levels, and markers of diastolic dysfunction, including higher E/e' ratio. Reduced RV strain was present in 18.9% of patients and was associated with a higher burden of traditional cardiovascular risk factors, including smoking, higher heart rate and diastolic blood pressure, and more adverse lipid profile, but not with inflammatory markers or disease activity. During follow-up, the incidence of ACE was low, and neither reduced LA nor RV strain was significantly associated with adverse outcomes. However, both LA and RV strain parameters showed significant correlations with abnormal markers of cardiac structure and function, including LV global longitudinal strain.

Conclusion: In RA patients without overt cardiovascular disease and preserved LV systolic function, most individuals exhibit normal LA and RV strain. Reduced LA strain is associated with worse functional capacity and elevated biomarker of cardiac dysfunction and inflammation-related disease activity, whereas reduced RV strain appears more closely linked to traditional cardiovascular risk factors. Although no independent prognostic value was demonstrated, myocardial deformation imaging may provide important insights into subclinical cardiac involvement in RA and help refine cardiovascular risk stratification in this population.

LIST OF ABREVIATIONS

ACE – Adverse cardiovascular events

ACEi – Angiotensin-converting enzyme inhibitor

AF- Atrial fibrillation

Anti-CCP – Anti-cyclic citrullinated peptide antibodies

ARB – Angiotensin II receptor blocker

ASE – American Society of Echocardiography

BMI – Body mass index

BSA – Body surface area

CCB – Calcium channel blocker

CI – Confidence interval

COPD – Chronic obstructive pulmonary disease

CVD – Cardiovascular disease

DAS28 – Disease Activity Score in 28 joints

DBP – Diastolic blood pressure

DD – Diastolic dysfunction

EF- Ejection fraction

eGFR – Estimated glomerular filtration rate

ESR- Erythrocyte sedimentation rate

ESC – European Society of Cardiology

EULAR – European League Against Rheumatism

GLS – Global longitudinal strain

HbA1c – Hemoglobin A1c

HDL – High-density lipoprotein

HF – Heart failure

HFpEF – Heart failure with preserved ejection fraction

HR – Hazard ratio **hsTnT –** High-sensitivity troponin T

IL-1 – Interleukin 1

IL-6 – Interleukin 6

IVC – Inferior vena cava

IVS – Interventricular septum

JAK/STAT – Janus kinase / Signal transducer and activator of transcription

LA – Left atrium

LACs – Left atrial conduit strain

LAPs – Left atrial pump strain

LARs – Left atrial reservoir strain

LAs – Left atrial strain

LDL – Low-density lipoprotein

LV – Left ventricle

LVEDD – Left ventricular end-diastolic diameter

LVEDV – Left ventricular end-diastolic volume

LVEF – Left ventricular ejection fraction

LVESD – Left ventricular end-systolic diameter

LVESV – Left ventricular end-systolic volume

LVFP – Left ventricular filling pressures

MRA – Mineralocorticoid receptor antagonist

NSAIDs – Non-steroidal anti-inflammatory drugs

NT-proBNP – N-terminal pro-brain natriuretic peptide

OAD – Oral anti-diabetic drugs

PASP – Pulmonary artery systolic pressure

PW – Posterior wall

RA – Rheumatoid arthritis

RF-IgM – Rheumatoid factor, immunoglobulin M type

SBP – Systolic blood pressure

SPSS – Statistical Package for the Social Sciences

TAPSE – Tricuspid annular plane systolic excursion

TNF-α – Tumor necrosis factor alpha

TR – Tricuspid regurgitation

6MWT – 6-minute walk test

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Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder characterized by joint involvement and multisystem pathology, that affects approximately 1–2% of the global population.[1] Cardiovascular disease (CVD) is currently the leading cause of excess mortality in RA. A comprehensive review of 50 studies including 91,618 patients and 33,250 deaths reported that 39.6% of fatalities were attributable to CVD.[2] Furthermore, this excess risk is not fully explained by traditional cardiovascular risk factors, as RA independently increases cardiovascular events by 48% and CVD-related mortality by 50% relative to the general population.[3] A US-based registry further demonstrated that reducing RA disease activity from high activity to remission was associated with an approximate 50% reduction in cardiovascular events. In recognition of this, the European League Against Rheumatism (EULAR) recommends applying a 1.5-fold multiplier to standard CVD risk algorithms when evaluating RA patients.[4]

Crowson et al. identified smoking and hypertension as carrying the highest population attributable risk in RA patients, with non-smokers exhibiting a 23% lower cardiovascular risk. Hypertension and diabetes mellitus are also more common in RA.[5] Although hypertension is a traditional cardiovascular risk factor, growing evidence implicates systemic inflammation, central to RA pathogenesis, in sustaining chronic elevated blood pressure.[6] RA patients are also more likely to exhibit insulin resistance, abnormal fat distribution and physical inactivity compared with non-RA controls.[7] Moreover, increased RA disease activity or duration independently predicts metabolic syndrome development.[8]

RA–associated myocardial disease is primarily driven by chronic systemic inflammation. Pro-inflammatory cytokines, including TNF-α, IL-1, and IL-6, promote endothelial dysfunction, oxidative stress, and activation of the renin–angiotensin–aldosterone system, leading to adverse ventricular remodeling.[9] Autoimmune activation further amplifies inflammation via macrophage activation and IL-6–dependent JAK/STAT signaling.[10,11] Microvascular dysfunction, impaired endothelial repair, and oxidative stress contribute to subclinical ischemia and myocardial fibrosis, increasing ventricular stiffness and predisposing to diastolic dysfunction (DD).[12]

Invariably, heart failure (HF) is a major complication in RA, driven by abnormalities in both systolic and diastolic function, with an approximately two-fold increased risk and a predominant phenotype of HF with preserved ejection fraction (HFpEF).[13] Disease activity markers such as ESR (Erythrocyte Sedimentation Rate), DAS28 (Disease Activity Score in 28 joints) and RF-IgM (Rheumatoid Factor, IgM type) are associated with impaired diastolic filling and reduced systolic performance, indicating a global effect of inflammation on myocardial function.

Although research in patients with RA has predominantly concentrated on the left ventricle (LV) and its systolic performance, the left atrium (LA) serves as an important indicator of persistently increased LV filling pressures (LVFP) and DD.[14,15] More recently, the evaluation of LA strain (LAs) using speckle-tracking

echocardiography (STE) has emerged as a valuable approach for assessing atrial function, diastolic properties, and indirectly estimating LVFP.[14] LAs comprises three phases corresponding to the atrial cycle: reservoir strain (LARs), conduit strain (LACs), and pump strain (LAPs). Left atrial reservoir strain (LARs) represents LA dilation during the reservoir phase of the atrial cycle (corresponding to ventricular systole), it is closely related to atrial compliance and is described as a percentage of myocardial stretching; LACs represents atrial dynamics during early ventricular diastole (where the LA serves as a "conduit" for pulmonary venous return); and LAPs corresponds to atrial systole (myocardial shortening) at ventricular end-diastole. Decreases in LARs and/or LAPs beyond established cut-off values correlate with elevated left ventricular filling pressure (LVFP) and are now integrated into contemporary algorithms for diastolic function evaluation.[16,17,18] Furthermore, diminished LAs has been associated with a higher likelihood of atrial fibrillation (AF) and stroke.[19]

In a prospective RA cohort without overt cardiovascular disease, impaired global longitudinal strain (GLS) was present in a substantial proportion of patients and independently predicted adverse cardiovascular outcomes, highlighting early myocardial involvement.[20] Nevertheless, within the RA population, LAs remains underexplored, with existing studies limited to relatively small cohorts.[15, 21] A decline in LAs has been suggested as an early indicator preceding reductions in LV GLS, and may serve as a useful screening parameter for the early detection of cardiac involvement in RA. This could facilitate the identification of individuals at increased risk for HF and other adverse clinical outcomes.[21]

Right ventricular systolic function is commonly evaluated using longitudinal velocities and structural displacement measures.[22] However, due to the developments in STE, right ventricle (RV) strain analysis has the potential to be a more sensitive marker of its systolic function.[23, 24, 25] RV strain is assessed from a right ventricle–focused apical four-chamber view, with segmentation of the RV free wall. RV GLS is calculated as the mean segmental longitudinal strain including the interventricular septum. RV free wall strain (FWS) excludes the interventricular septum and might be preferred as it reflects exclusively the RV myocardial function.[26]

Contemporary 2025 ASE (American Society of Echocardiography) guidelines for right heart evaluation, emphasize the integration of myocardial deformation parameters into routine assessment, reflecting a shift from purely geometry- and Doppler-based indices toward a more comprehensive approach.[22] Although primarily focused on left-sided assessment, this paradigm reinforces the value of deformation imaging in identifying subtle biventricular involvement in systemic diseases such as RA. As such, in addition to the role of LA strain, data suggest the clinical relevance of right RV strain in the evaluation of subclinical RV systolic dysfunction in RA. Previous observational studies have demonstrated, lower absolute RV GLS in modestly sized samples of RA patients.[27] Concurrently, RV involvement in RA is increasingly recognized as a manifestation of heart disease in this population, but its association with clinical outcomes is yet to be demonstrated.

In the present study, we aim to characterize LA and RV dynamics in RA patients without overt CVD and preserved LV systolic function and to investigate their prognostic significance in this selected population. Specifically, we assessed the association between LA and RV strain values and the incidence of adverse cardiovascular events, disease activity indices, inflammatory biomarkers, and other echocardiographic parameters, including diastolic function and LV filling pressures. By focusing on a population without systolic dysfunction, this study seeks to clarify the role of LA and RV strain as early, non-invasive markers of subclinical cardiac involvement in rheumatoid arthritis.

Methods

Summary of the study design

This was a single-center retrospective study including patients from the Autoimmune Diseases Clinic at a tertiary care university hospital in Porto, Portugal. Patients aged 18 years or older, observed between June 2016 and June 2018, who had previous diagnosis of RA, and that subsequently underwent systematic echocardiographic evaluation, were screened. Clinical outcome data was retrospectively collected up to 7 years of follow-up. This study complies with the Declaration of Helsinki and the study protocol was reviewed and approved by the local institutional ethics committee with the number 025.247 (205-CAC205-CE).

Panent selection

The study included patients with RA, according to the 2010 ACR/EULAR Classification Criteria,[4] and no prior formal diagnosis of heart disease or evidence of LV systolic dysfunction. Patients observed at the Autoimmune Disease Clinic ambulatory appointments, between 2016 and 2018, were prospectively and consecutively proposed to enroll in this study. In those who accepted to participate, immediate clinical evaluation, blood collection for analyses, electrocardiogram and 6-minute walk test were done; they were referred for systematic echocardiographic evaluation subsequently. Patients with severe comorbidities, active malignancy, dementia, expected survival of less than 6 months, inability to walk, complete dependance on activities of daily living, and without echocardiographic evaluation were excluded. For the present analysis, exclusion criteria also comprised: history of coronary artery or severe valvular disease, previous diagnosis of HF; atrial fibrillation (AF), reduced Left ventricular ejection fraction LVEF (< 50%) or LV GLS (> -16%) at the time of the echocardiogram. Patients with poor image quality preventing acceptable LAs analysis were excluded. Specifically for the RV strain focused analysis, patients with inacceptable image quality for accurate RV strain analysis were also excluded (Figure 1).

Definitions and data collection

Clinical data, laboratory, imaging and other exam results were obtained through hospital digital clinical records. These included: vital signs, body-mass index, a 12-lead electrocardiogram and a 6-minute walk test (6MWT) result at the time of the index ambulatory evaluation (before echocardiographic evaluation). At the same moment, serum biomarker analysis was preformed including: hemogram, serum creatinine, glycated hemoglobin, lipid profile, high-sensitivity troponin T (hsTnT), N-terminal pro-brain natriuretic peptide (NT-proBNP), C-reactive protein, erythrocyte sedimentation rate (ESR), ferritin and anti-cyclic citrullinated peptides antibodies (anti-CCP) and rheumatoid factor. Estimated glomerular filtration rate was obtained through the Chronic Kidney Disease Epidemiology Collaboration 2021 formula.[28]

Echocardiographic evaluation was performed by a trained cardiologist specialized in cardiovascular (CV) imaging. The exams were performed using a Philips® iE33 ultrasound machine. Cardiac chamber dimensions (LA and LV volumes calculated via Simpson's biplane method), LV wall thickness and mass, LVEF

(determined by the modified Simpson's biplane method), valvular disease, pericardial disease, and diastolic function parameters (as recommended in the European Society of Cardiology (ESC) 2016 guidelines)[14] were assessed and indexed for body-surface area when appropriate. Two other cardiologists and a medical student were responsible for post-hoc LV, LA and RV strain analysis using the vendor independent software TomTec® (IntelliSpace Cardiovascular, Philips Medical Systems), according to European Association of Cardiovascular Imaging/American Society of Echocardiography recommendations.[22, 29] LV GLS analysis methodology has been previously described.[20] LA strain analysis was performed using the same vendor independent software (TomTec®). LARs, LACs and LAPs were automatically computed through 2D-speckle-tracking analysis of a 4-chamber view cine loop, acquired with R-R interval electrocardiographic gating. The endocardial border of the LA was automatically traced and manually adjusted (when needed) at end-systole, and the region of interest was automatically adjusted to include the atrial myocardium. Longitudinal strain curves were generated, and strain values were derived based on atrial deformation timing within the cardiac cycle, using R-R gating as the reference. Myocardial tracking quality was visually assessed by the responsible cardiologist (Figure 2). Cases with inadequate image quality were excluded from the analysis. RV strain was also obtained from a single 4-chamber view cine loop using the same semi-automated vendor independent software. The endocardial border of the RV was automatically traced and manually adjusted (if needed), generating longitudinal strain curves and yielding peak RV FWS and RV GLS (which averages the interventricular septum peak longitudinal strain and the RVFWs) values (Figure 3). Also, myocardial tracking was visually assessed by the responsible cardiologist and cases with inadequate image quality were excluded from the subsequent RV focused analysis. The patients were classified into DD groups according the 2024 British Society of Echocardiography (BSE) criteria.[30] When coding the echo findings, the cardiologists were blinded to clinical data and outcomes.

Main outcomes and exploratory analysis

This study comprises two main analyses: first, evaluation of cardiovascular outcomes according to LA strain; second, evaluation of cardiovascular outcomes according RV strain, after excluding those with inadequate image quality for the later analysis. The study subjects were initially divided into two groups according to LA strain values, categorized as low (LARs and/or LAPs below age and sex-adjusted reference thresholds) or normal, according to previously published cut-off values in Table 3 of *Singh A, Carvalho Singulane C, Miyoshi T, et al. Normal Values of Left Atrial Size and Function and the Impact of Age: Results of the World Alliance Societies of Echocardiography Study. J Am Soc Echocardiogr 2022;35:154–164.e3*.[31] Baseline and echocardiographic characteristics, and the incidence of the primary and secondary outcomes were compared between them. Afterwards, excluding the patients with insufficient image quality for RV strain analysis, the cohort was divided into two groups according to the RV strain values, categorized as low RV strain (RV GLS < 17% or RVFWs < 20%) or normal, according to previously published cut-off values in 2025 by Mukherjee et al.[22] Baseline and echocardiographic characteristics, and the incidence of the primary and secondary outcomes were also compared between them.

The primary outcome was adverse CV events (ACE), a composite endpoint including myocardial infarction, stroke, CV death, HF hospitalization (hospitalization of at least 24 hours due to decompensated HF), and AF (clinical AF episode per European Society of Cardiology guidelines definition).[32] Secondary endpoints included the individual ACE components (CV death, HF hospitalization, AF) and all-cause mortality.

Finally, to understand the relationship between the LARs, RVs, disease biomarkers, activity indices and cardiac structural/functional parameters, we analyzed the correlations between LARs and age, DAS28, disease duration, 6MWT distance, NT-proBNP, E/e' ratio; ESR, LV GLS, RV GLS, and tricuspid annular plane systolic excursion (TAPSE). Correlations between RV GLS and age, DAS28, disease duration, 6MWT distance, NT-proBNP, serum creatinine, C-reactive protein, e' septal, LV GLS, LARs, s' tricuspid annulus and TAPSE were also computed. Adjustments for covariates were made whenever the index correlation was statistically significant.

Statistical analysis

Statistical analysis was performed using IBM software Statistical Package for Social Sciences (SPSS) version 29.0. Continuous variables were described using mean (standard deviation) or median (percentile 25 – percentile 75), depending on the normality of the distribution. For normally distributed variables, means were compared using the student's t-test, while medians (for non-normally distributed variables) were compared using Mann-Whitney-U test. Categorical variables were described with absolute numbers and proportions (%) and compared using Chi-square and Fisher's exact test, as appropriate. Survival analyses were performed using the Kaplan-Meier survival curves (Log Rank test) and Cox proportional hazards models to obtain hazard ratios (HR) and the corresponding 95% confidence intervals. Pearson correlations were used to analyze the relationship between LARs and RV GLS with disease parameters, echocardiographic variables, and biomarkers. Covariates with a significant association in the univariate analysis (*p-value* < 0.05) entered the multivariate stage, where partial correlations controlling for age and sex were computed. A two-tailed p-value < 0.05 was considered statistically significant.

Results

Baseline demographic and clinical characteristics according to LAs

Of the 408 patients initially screened, 364 were enrolled, after exclusions according to the criteria previously described, and underwent echocardiographic evaluation. Of those, 86 were excluded due to previously known heart disease or systolic dysfunction documented in the echocardiographic analysis. Finally, 18 were also excluded due to insufficient image quality for LAs analysis. The final cohort included 260 patients, with a mean age of 53.9 (± 13.5) years, and 82% of female sex. Of these, 22 had low LAs and 238 had normal LAs (Table I, Figure 1). Patients with low LAs were older compared to those with normal LAs (61.9 ± 12.4 vs. 55.4 ± 13.1 years, p = 0.026). No significant differences were observed regarding sex distribution, body mass index, blood pressure, heart rate, or QRS duration. Functional capacity was significantly reduced in patients with low LAs, who presented shorter distances in the 6-minute walk test (313 ± 120 vs. 389 ± 72.5 m, p = 0.010). Regarding comorbidities, there were no statistically significant differences between groups, although a higher prevalence of chronic kidney disease and diabetes mellitus was observed in the low LAs group. Patients with low LAs also had higher disease activity, as reflected by higher DAS28-ESR (3.62 ± 1.75 vs. 2.76 ± 1.14, p = 0.049). Laboratory analysis showed that patients with low LAs had lower hemoglobin levels (12.1 ± 1.46 vs. 13.3 ± 1.32 g/dL, p < 0.001), higher NT-proBNP levels (108 [58.2–264] vs. 68.4 [39.2–117] pg/mL, p = 0.006), and higher ESR values (33.2 ± 24.5 vs. 23.5 ± 17.8 mm/h, p = 0.041). No significant differences were observed in renal function, lipid profile, or C-reactive protein concentrations.

Echocardiographic characteristics according to LAs groups

Echocardiographic parameters are summarized in Table II. LA and ventricle dimensions, volumes, and ejection fraction (EF) were similar between groups. However, patients with low LAs had higher median E/e' ratio (9.70 [8.38–11.7] vs. 8.05 [6.60–9.00], p = 0.004). No significant differences were found in right ventricular size or conventional systolic parameters, although a trend toward lower TAPSE values was observed in the low LAs group. Considering the whole sample, the mean LARs, LACs and LAPs were 37.6%, -20,0% and -17.5%, respectively. Mean LARs was 24.0% in the low LAs group, and 38.9% in normal LAs group. The prevalence of DD was numerically higher among patients with low LAs, particularly with indirect signs of elevated LVFP.

Primary and secondary outcomes according to LAs

During follow-up, the incidence of the primary composite endpoint (ACE) occurred in 20 patients, 2 (9.1%) in patients with low LAs and 18 (7.6%) in patients with normal LAs (HR 1.31 [0.31–5.66], p = 0.715) (Table III, Figure 4). No significant differences were observed in secondary outcomes, including cardiovascular death, heart failure hospitalization, atrial fibrillation, or all-cause mortality.

Correlations between LARs and clinical, laboratory, and echocardiographic parameters

LARs showed significant, albeit weak, correlations with several clinical and echocardiographic variables (Table IV). Age (r = -0.387, p < 0.001), NT-proBNP (r = -0.248, p < 0.001), E/e' ratio (r = -0.303, p < 0.001), LV GLS (r = -0.304, p < 0.001) and RV GLS (r = -0.243, p = 0.001) were negatively correlated with LARs, while 6MWT distance (r = 0.216, p < 0.001) and TAPSE (r = 0.134, p = 0.031) were positively correlated. After adjustment for age and sex, LARs remained significantly correlated with NT-proBNP (r = 0.145, p = 0.021), E/e' ratio (r = -0.150, p = 0.016), left ventricular global longitudinal strain (r = -0.253, p < 0.001), right ventricular GLS (r = -0.216, p = 0.004), and TAPSE (r = 0.139, p = 0.026).

Baseline demographic and clinical characteristics according to RV strain

Due to insufficient image quality for RV strain evaluation, 80 patients were excluded from this analysis. A subgroup of 180 patients was categorized according to right ventricular strain (RVs), into low RVs (n = 34) and normal RVs (n = 146) groups (Table V, Figure 1). The low RVs group had a lower prevalence of female patients (61.8% vs. 86.3%, p < 0.001) and had higher mean heart rate (82.1 ± 14.5 vs. 77.0 ± 11.7 bpm, p = 0.031). Tobacco use was also more prevalent in this group (52.9% vs. 30.8%, p = 0.015). Laboratory findings showed higher hemoglobin (13.6 ± 1.06 vs. 13.0 ± 1.37 g/dL, p = 0.030), creatinine (0.80 ± 0.20 vs. 0.73 ± 0.15 mg/dL, p = 0.026), and LDL cholesterol concentrations (121 ± 40.1 vs. 95.8 ± 28.5 g/dL p < 0.001) in patients with low RVs.

Echocardiographic characteristics according to RV strain

Echocardiographic findings are presented in Table VI. In the overall sample mean RV GLS and FWs were 26.4% and -22.1%, respectively. Patients with low RVs had lower septal and lateral e' velocities (p < 0.001 and p = 0.008, respectively). Left ventricular systolic function was also inferior in this group, as reflected by lower absolute LV GLS (-19.1% vs -21.3%, p < 0.001), although LVEF remained comparable between the groups.

Primary and secondary outcomes according to RV strain

The incidence of the ACE was numerically higher, but not significantly different in patients with low RVs compared to those with normal RVs (11.8% vs. 5.5; HR 2.28 [0.685–7.56], p = 0.179) (Table VII, Figure 5). No significant differences were observed in the secondary outcomes.

Correlations between RV GLS and clinical and echocardiographic parameters

RV GLS correlated significantly with several echocardiographic parameters (Table VIII). Positive, however moderate to weak, correlations were observed with LV GLS ($r = 0.396$, $p < 0.001$) and age ($r = 0.169$, $p = 0.023$), while negative weak correlations were found with septal e' velocity ($r = -0.302$, $p < 0.001$), TAPSE ($r = -0.200$, $p = 0.007$), and S' tricuspid annulus ($r = -0.173$, $p = 0.023$). RV GLS was also negatively correlated with LARs ($r = -0.243$, $p = 0.001$). After adjustment for age and sex, all the previous correlations maintained their statistical significance.

Discussion

The main findings of the present study are: (1) in a selected RA population without over cardiac disease and preserved LV systolic function, left atrial and right ventricular strain are normal in the majority of patients (92% and 81%, respectively); (2) patients with reduced LAs had reduced functional capacity (lower 6MWT distance), higher disease activity score, inflammatory biomarkers, and markers cardiac dysfunction: higher E/e' and increased NT-proBNP concentrations; (3) in individuals with reduced RV strain, there was no indication of higher inflammatory activity or worse functional status, but they displayed a higher prevalence of traditional cardiovascular risk factors, including higher diastolic blood pressure, smoking prevalence, and a more adverse lipid profile; (4) despite these surrogate findings, left atrial and right ventricular strain were not significantly associated with clinical outcomes.

This study is embedded within a broader, structured research program based on a large, prospectively characterized cohort, from which multiple complementary analyses have been derived.[33] This approach has enabled a stepwise and integrated evaluation of cardiovascular involvement, with each study building upon previous findings to refine the understanding of cardiac dysfunction using consistent methodology and a well-defined population. Prior work has demonstrated a substantial burden of subclinical ventricular dysfunction — including both systolic and diastolic abnormalities —and its association with impaired functional capacity and adverse biomarker profiles. Complementary studies have further shown that HF is frequently underdiagnosed and is driven by a complex interplay between systemic inflammation and traditional cardiovascular risk factors.[20] This group has later showed that subclinical left ventricular systolic dysfunction, identified by reduced left ventricular GLS, was strongly associated with adverse cardiovascular events in RA.[20] The present study extends prior analyses by incorporating myocardial deformation imaging across cardiac chambers, beyond LV GLS. Previous investigations focused on left ventricular systolic and diastolic function, as well as their prognostic implications, establishing a foundation for the evaluation of more sensitive markers of early myocardial dysfunction. In this paper, LA and RV strain, were explored, consisting of the largest RA cohort to date reporting on these parameters.

Focusing on the pathophysiological perspective of our findings, chronic inflammation in RA promotes myocardial fibrosis, endothelial dysfunction, and microvascular impairment, leading to increased LV stiffness and impaired relaxation. These alterations may directly affect LA mechanics, resulting in reduced atrial deformation even in the absence of overt cardiac disease. Accordingly, LA dysfunction appears to reflect inflammation-driven myocardial remodeling and early diastolic impairment.

LA strain has emerged as a sensitive and reproducible marker of atrial function and its interaction with LV diastolic mechanics.[26] LARs is the most clinically informative component, reflecting atrial compliance during ventricular systole while integrating the effects of LV relaxation, stiffness, and filling pressures. Reduced LARs correlates with invasively measured LV filling pressures and provides incremental diagnostic value over conventional parameters.[18, 35]

Beyond its diagnostic utility, LA strain also carries prognostic value. Reduced values—particularly below 18%—have been associated with incident atrial fibrillation and histologically confirmed fibrosis, linking impaired atrial mechanics to arrhythmogenesis.[36] Further analysis of conduit and contractile strain enables the detection of subtle atrial dysfunction, including patterns of atrial myopathy.[37] Compared with structural parameters, such as left atrial volume index (LA strain offers greater sensitivity for early dysfunction and correlates with LV diastolic impairment independently of atrial size,[38, 39] despite its assessment requiring high-quality imaging and standardized acquisition.[40] Besides, these alterations may be partially reversible. Anti-inflammatory therapies—particularly anti–TNF-α agents—have been associated with improvements in LA strain and reductions in LV filling pressures, suggesting that inflammation-driven myocardial dysfunction may be modifiable,[41] which opens the door for prognostic impact of early dysfunction diagnosis.

The present findings are consistent with prior studies demonstrating subclinical myocardial dysfunction in RA, while highlighting a lower prevalence and milder phenotype in contemporary cohorts. Ji et al. reported significant and progressive reductions in LA strain parameters across disease stages,[15] whereas in our study only 8.5% of patients exhibited reduced LA strain, with mean values remaining largely within normal ranges (Table II), likely reflecting a more benign and selected population. Similarly, Baktir et al. showed impaired myocardial deformation despite preserved conventional echocardiographic parameters,[42] a finding mirrored in our cohort, reinforcing the sensitivity of strain imaging for early dysfunction. In line with Cho et al., reduced LA strain in our study was associated with higher E/e' and NTproBNP levels, supporting its role as a marker of early diastolic impairment.[43]

Considering clinical outcomes, the overall incidence of ACE was low, likely reflecting the selected nature of the cohort. Although higher event rates were observed in patients with lower LARs, statistical significance was not reached, possibly due to limited event numbers and follow-up duration. Previous analyses demonstrated an association between reduced LV GLS and increased risk of major adverse events[20]. In contrast, the present study excluded patients with prior HF or LV systolic dysfunction, representing a lower-risk population and potentially explaining the lower event rates.

Regarding RV parameters, strain analysis enabled the identification of a subgroup characterized by adverse clinical, biochemical, and echocardiographic features. The sample size for RV analysis (n = 180) is substantially larger than those reported in prior studies, including Aquino et al. (n = 34) and Fine et al. (n = 87), and comparable to Naseem et al. (n = 120).[27,34,44]

In the present cohort, a relatively low proportion of patients exhibited subclinical RV dysfunction, with 34 (19%) individuals classified as having reduced RV strain. Overall, our findings are more similar than different compared with previous studies, at least from a qualitative perspective. As demonstrated by Fine et al., patients with RA exhibited reduced RV GLS despite preserved LVEF, suggesting early subclinical myocardial involvement[44]. Similarly, Aquino et al. reported impaired RV function, including reduced RV FWS and altered right ventriculoarterial coupling.[34] Despite this qualitative agreement, quantitative differences in the magnitude of strain reduction exist between studies. These differences are likely multifactorial. First, our cohort shows relatively low inflammatory activity (mean DAS28-ESR ~2.8), which may reflect better disease control and consequently a lower degree of myocardial involvement, in contrast to other populations with higher inflammatory burden. Second, there are important differences in the parameters assessed: Fine et al. evaluated global RV longitudinal strain, whereas Aquino et al. focused on RV free-wall strain and derived indices such as ventriculoarterial coupling, which are not directly comparable and may be more sensitive in detecting early dysfunction. Additionally, methodological variability inherent to speckle tracking echocardiography (including software, vendor, and segment definition, particularly septal inclusion) can significantly influence absolute strain values.

Notably, reduced RV strain in our cohort was associated with a distinct clinical profile characterized by lower female prevalence, higher heart rate and diastolic blood pressure, increased tobacco exposure, and a more adverse metabolic profile, including higher concentrations of LDL cholesterol. This contrasts with prior studies emphasizing inflammation and disease activity as primary drivers of myocardial dysfunction in RA. For example, Naseem et al. reported strong correlations between RV strain and disease activity scores, whereas no such associations were observed in the present study.[27] These findings suggest that, in well-controlled RA populations, traditional cardiovascular risk factors and systemic comorbidity burden may play a more prominent role in myocardial impairment than inflammatory activity *per se.*

Mechanistically, our results further support the concept that RV dysfunction reflects global myocardial involvement rather than isolated right-sided disease. Patients with reduced RV strain also exhibited impaired LV deformation, reduced septal and lateral e' velocities, and alterations in diastolic timing parameters, indicating early DD. Moreover, RV GLS correlated with LV GLS and LARs, highlighting ventricular–atrial coupling and diffuse myocardial impairment. These observations are consistent with prior reports of biventricular involvement while reinforcing the concept of a multichamber functional continuum.[44]

Finally, the present study extends the existing literature by incorporating outcome assessment. Previous studies evaluating RV strain in RA have been largely cross-sectional, without systematic evaluation of clinical endpoints.[27,34] In contrast, we observed a numerically higher incidence of adverse cardiovascular events in patients with reduced RV strain (11.8% vs. 5.5%), although this difference did not reach statistical significance. It is important to note that normal reference ranges for RV strain parameters are relatively wide,[23, 45] which may complicate the identification of clinically meaningful thresholds. Our methodological decision to dichotomize the cohort into normal versus reduced RV strain groups aimed to isolate a clearly abnormal subgroup and enhance specificity; however, given that RV strain is inherently a continuous variable, this approach may have reduced statistical power to detect differences in outcomes. Although probably underpowered, these findings suggest a potential prognostic role of RV strain in RA and are in line with broader cardiovascular literature linking impaired RV deformation to adverse clinical outcomes.

Limitations

This study has several limitations that should be considered when interpreting the results. First, although the cohort was originally established using a prospective design, the strain measurements and outcome reporting were analyzed retrospectively, which may have introduced bias. Second, the lack of a matched healthy control group limits direct comparison with the general population, and it remains possible that some of the observed findings are not specific to AR but instead represent patterns also seen in individuals without disease. Third, because enrollment depended on patients agreeing to participate, selection bias cannot be excluded, as participants may differ in relevant ways from those who did not take part. Fourth, several patients were excluded because image quality was insufficient for reliable analysis, particularly for right ventricular evaluation, which is technically more challenging and was not the primary focus of the original imaging protocol. Fifth, although the long follow-up period is an important strength, changes in treatment strategies or patient characteristics during follow-up were not systematically documented. Sixth, the use of dichotomized echocardiographic variables may have limited the ability to identify more subtle relationships or progressive risk gradients. Finally, the relatively low number of clinical events may have reduced the statistical power to detect significant differences between groups.

Conclusion

In conclusion, 8.5% and 18.9% of RA patients with no overt cardiac disease have reduced LA and RV strain respectively. Low LAs was associated with reduced functional capacity, higher disease activity scores, and increased NT-proBNP concentrations, whereas reduced RV strain was linked to a more adverse cardiovascular risk profile. While deformation imaging, particularly left ventricular strain, shows promise for the early detection and phenotypic characterization of cardiac involvement in RA, left atrial and right ventricular strain were not independently associated with clinical prognosis in our cohort of patients with a low rate of adverse events.

Appendix

Tables

Table I. Characterization of the studied subgroups according to LA strain.

General features	Low LAs (n = 22)	Normal LAs (n = 238)	Overall (n = 260)	p value
Age (years)	61.9 (± 12.4)	55.4 (± 13.1)	56.0 (± 13.2)	**0.026**
Sex (female)	19 (86.4)	190 (79.8)	209 (80.4)	0.583
BMI (Kg/m^2)	26.7 (± 5.16)	26.2 (± 4.21)	26.3 (± 4.29)	0.649
BSA (m^2) *	1.63 [1.60 – 1.80]	1.70 [1.60 – 1.80]	1.70 [1.60 – 1.80]	0.228
SBP (mmHg)	134 (± 24.9)	131 (± 18.5)	132 (± 19.1)	0.553
DBP (mmHg)	74.6 (± 12.0)	75.7 (± 10.2)	75.6 (± 10.3)	0.642
Heart rate (bpm)	77.6 (± 8.05)	78.5 (± 13.0)	78.5 (± 12.6)	0.610
Sinus rhythm	22 (100)	238 (100)	260 (100)	-
QRS duration (ms) *	90.5 [82.0 – 96.8]	91.0 [85.0 – 100]	90.5 [85.0 – 100]	0.459
6MWT distance (m)	313 (± 120)	389 (± 72.5)	382 (± 80.1)	**0.010**
Comorbidities and cardiovascular risk factors				
History of stroke	1 (4.50)	3 (1.30)	4 (1.50)	0.299
COPD	1 (4.50)	10 (4.20)	11 (4.20)	0.939
Chronic kidney disease	2 (9.10)	3 (1.30)	5 (1.90)	0.059
Diabetes mellitus	5 (22.7)	24 (10.1)	29 (11.2)	0.081
Hypertension	10 (45.5)	95 (39.9)	105 (40.4)	0.612
Dyslipidemia	13 (59.1)	99 (41.6)	112 (43.1)	0.113
Obesity	5 (22.7)	40 (16.8)	45 (17.3)	0.554
Tobacco smoking	7 (31.8)	80 (33.6)	87 (33.5)	0.864
RA duration (years)	13.6 (± 9.13)	10.4 (± 9.8)	10.7 (± 9.77)	0.136
DAS28-ESR	3.62 (± 1.75)	2.76 (± 1.14)	2.84 (± 1.22)	**0.049**
RA medication				
NSAIDs	7 (31.8)	64 (26.9)	71 (27.3)	0.620
Corticosteroids	10 (45.5)	95 (39.9)	105 (40.4)	0.612
Methotrexate	13 (59.1)	151 (63.4)	164 (63.1)	0.686
Biologics	4 (18.2)	47 (19.7)	51 (19.6)	0.860
Others	7 (31.8)	101 (42.4)	108 (41.5)	0.334
Chronic medication				
Insulin	3 (13.6)	12 (5.00)	15 (5.80)	0.684
OAD	4 (18.2)	19 (8.00)	23 (8.80)	0.967
ACEi/ARB	8 (36.4)	75 (31.5)	83 (31.9)	0.641
Beta-blocker	3 (13.6)	12 (5.00)	15 (5.80)	0.123
CCB	2 (9.10)	23 (9.70)	25 (9.60)	0.930
MRA	0 (0.00)	1 (0.40)	1 (0.40)	-
Thiazide diuretic	2 (9.10)	35 (14.7)	37 (14.2)	0.750
Loop diuretic	1 (4.50)	2 (0.80)	3 (1.20)	0.234
Statin	11 (50.0)	74 (31.1)	85 (32.7)	0.070
Laboratory serum parameters				
Hemoglobin (g/dL)	12.1 (± 1.46)	13.3 (± 1.32)	13.2 (± 1.37)	**< 0.001**

Leucocytes (x10^9/L)	6946 (± 1984)	6953 (± 2080)	6953 (± 2068)	0.989
Creatinine (mg/dL)	0.73 (± 0.14)	0.76 (± 0.16)	0.76 (± 0.17)	0.407
eGFR (ml/min/1.73m^2) **	90.3 (± 18.2)	91.8 (± 18.7)	91.7 (± 18.6)	0.715
HbA1c (%) *	5.50 [5.18 – 5.80]	5.40 [5.10 – 5.70]	5.40 [5.10 – 5.70]	0.430
Total cholesterol (mg/dL)	193 (± 44.0)	186 (± 35.0)	187 (± 36.0)	0.399
LDL cholesterol (mg/dL)	104 (± 41.1)	101 (± 29.8)	101 (± 30.8)	0.702
HDL cholesterol (mg/dL)	66.4 (± 15.7)	60.6 (± 16.8)	61.1 (± 16.8)	0.117
HsTnT (mg/mL) *	0.004 [0.002 – 0.012]	0.004 [0.002 – 0.006]	0.004 [0.002 – 0.006]	0.468
NT-ProBNP (pg/mL) *	108 [58.2 – 264]	68.4 [39.2 – 117]	71.5 [40.2 – 122]	**0.006**
ESR (mm/h)	33.2 (± 24.5)	23.5 (± 17.8)	24.1 (± 18.3)	**0.041**
C-reactive protein (mg/L) *	4.14 [1.05 – 9.31]	2.91 [1.10 – 6.62]	2.83 [1.09 – 6.72]	0.335
Ferritin (ng/mL) *	139 [48.0 – 207]	94.0 [45.0 – 172]	101 [46.0 – 191]	0.319
Anti-CCP or rheumatoid factor (positive)	18 (81.8)	184 (77.3)	202 (77.7)	0.792

6MWT = 6 minute walk test; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; BSA = body surface area; CCB = calcium channel blocker; CCP = cyclic citrullinated peptides; COPD = chronic obstructive pulmonary disease; DAS28-ESR = Disease Activity Score 28 using ESR; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; ESR = erythrocyte sedimentation rate; HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; HsTnT = high-sensitivity troponin T; LA = left atrium; LAs = left atrium strain; LDL = low-density lipoprotein; MRA = mineralocorticoid receptor antagonist; NSAIDs = non-steroidal anti-inflammatory drugs; OAD = oral anti-diabetic; NT-Pro-BNP = N-terminal pro-brain natriuretic peptide; RA = rheumatoid arthritis; SBP = systolic blood pressure; SD = standard deviation.

Values correspond to mean (SD) or n (%) where appropriate.

Low left atrium strain refers to low reservoir or pump strain based on the cut-offs reported in table 3 of Singh A, Carvalho Singulane C, Miyoshi T, Prado AD, Addetia K, Bellino M, et al. Normal Values of Left Atrial Size and Function and the Impact of Age: Results of the World Alliance Societies of Echocardiography Study. J Am Soc Echocardiogr 2022;35:154–164.e3. doi: 10.1016/j.echo.2021.08.008.

* Variable with a non-normal distribution. Values correspond to median [percentile 25 – percentile 75]. ** eGFR using the CKD-EPI formula: Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. N Engl J Med 2021;385:1737–1749. doi:10.1056/NEJMoa2102953.

Table II. Echocardiographic parameters according to LA strain groups.

	Low LAs (n = 22)	Normal LAs (n = 238)	Overall (n = 260)	p value
Aortic stenosis				
Mild	3 (13.6)	20 (8.40)	23 (8.90)	-
Moderate	0 (0.00)	4 (1.70)	4 (1.60)	-
Aortic regurgitation				
Mild	1 (4.50)	13 (5.50)	14 (5.40)	-
Moderate	0 (0.00)	2 (0.80)	2 (0.80)	-
Mitral stenosis				
Mild	0 (0.00)	1 (0.40)	1 (0.40)	-
Mitral regurgitation				
Mild	10 (45.5)	85 (35.7)	95 (36.8)	-
Moderate	0 (0.00)	3 (1.30)	3 (1.20)	-
Pericardial effusion	0 (0.00)	3 (1.20)	3 (1.20)	-
IVC diameter (mm)	15.6 (± 2.47)	15.6 (± 2.84)	15.6 (± 2.81)	0.992
IVS thickness (mm)	8.64 (± 1.79)	8.46 (± 1.94)	8.48 (± 1.92)	0.685
PW thickness (mm)	8.36 (± 1.76)	7.90 (± 1.55)	7.94 (± 1.57)	0.184
LV mass indexed (g/m^2)	70.8 (± 19.5)	65.6 (± 18.6)	66.1 (± 18.7)	0.212
LVEDD (mm)	44.4 (± 3.96)	43.9 (± 4.98)	44.0 (± 4.90)	0.696
LVESD (mm)	28.8 (± 3.98)	28.6 (± 6.06)	28.6 (± 5.91)	0.870
LVEDV indexed (mL/m^2)	45.9 (± 9.27)	48.6 (± 12.3)	48.5 (± 12.2)	0.321
LVESV indexed (mL/m^2)	16.5 (± 4.55)	18.3 (± 5.38)	18.1 (± 5.33)	0.133
Stroke volume indexed (mL/m^2)	40.1 (± 10.6)	39.5 (± 9.72)	39.6 (± 9.78)	0.805
Cardiac output (L/min)	4.45 (± 1.07)	4.93 (± 1.30)	4.89 (± 1.28)	0.118
LVEF (%)	62.3 (± 5.07)	62.5 (± 5.90)	62.5 (± 5.83)	0.916
LA area (cm^2)	20.2 (± 2.84)	18.5 (± 3.73)	18.6 (± 3.67)	**0.031**
LA volume indexed (mL/m^2)	34.2 (± 7.65)	31.4 (± 9.35)	31.7 (± 9.24)	0.183
RA area (cm^2)	15.2 (± 3.24)	13.9 (± 2.90)	14.1 (± 2.95)	0.052
RV basal diameter (mm) *	29.0 [25.0 – 38.0]	30.0 [24.0 – 40.0]	30.0 [24.0 – 40.0]	0.698
Mitral E wave (cm/s)	78.6 (± 16.3)	73.1 (± 17.1)	73.6 (± 17.1)	0.154
Mitral E/A ratio *	0.98 [0.78 – 1.20]	0.96 [0.80 – 1.20]	0.96 [0.80 – 1.20]	0.920
Mitral E wave DT (ms)	143 (± 36.0)	152 (± 44.7)	151 (± 44.0)	0.327
Ar-A duration (ms)	-9.52 (± 30.7)	-11.4 (± 24.3)	-11.3 (± 24.8)	0.737
IVRT (ms)	89.5 (± 17.3)	90.6 (± 18.4)	90.5 (± 18.2)	0.795
e' septal (cm/s)	7.18 (± 2.80)	7.85 (± 2.35)	7.79 (± 2.39)	0.214
e' lateral (cm/s)	9.82 (± 2.91)	11.0 (± 3.38)	11.0 (± 3.36)	0.089
E/e' average *	9.70 [8.38 – 11.7]	8.05 [6.60 – 9.00]	8.30 [6.70 – 10.0]	**0.004**
e' < LLN for age **	3 (13.6)	17 (7.10)	20 (7.70)	0.236
S' tricuspid annulus (cm/s)	14.8 (± 3.17)	14.3 (± 2.76)	14.3 (± 2.80)	0.452
TAPSE (mm) *	22.5 [21.0 – 25.3]	24.0 [22.0 – 27.0]	24.0 [22.0 – 27.0]	0.088
TR maximum velocity (m/s)	2.40 (± 0.47)	2.22 (± 0.33)	2.24 (± 0.35)	0.069
PASP (mmHg) *	25.0 [20.0 – 28.0]	23.0 [19.0 – 26.0]	23.0 [19.0 – 26.0]	0.194
LV GLS (%)	-20.1 (± 2.53)	-20.7 (± 2.55)	-20.7 (± 2.55)	0.297
Normal Borderline	16 (72.7) 4 (18.2)	188 (79.0) 33 (13.9)	204 (78.5) 37 (14.2)	0.522

LA reservoir strain	24.0 (± 9.54)	38.9 (± 9.76)	37.6 (± 10.6)	-

Low (according to age) ***	13 (59.1)	0 (0.00)	13 (5.00)	-
LA conduit strain	-16.7 (± 11.6)	-20.3 (± 9.42)	-20.0 (± 9.65)	-
LA pump strain	-7.31 (± 4.77)	-18.4 (± 6.74)	-17.5 (± 7.28)	-
Low (according to age) ***	14 (63.6)	0 (0.00)	14 (5.40)	-
RV FW strain	-25.4 (± 7.29)	-26.5 (± 6.08)	-26.4 (± 6.15)	0.553
Low ****	2 (9.1)	25 (10.5)	27 (10.4)	1.000
RV GLS	- 20.7 (± 5.26)	- 22.2 (± 4.53)	- 22.1 (± 4.58)	0.265
Low ****	3 (13.6)	25 (10.5)	28 (10.8)	0.403
Diastolic dysfunction (2024) *****				
Yes, with elevated LVFP	4 (18.2)	5 (2.10)	9 (3.50)	-
Yes, with normal LVFP	2 (9.10)	17 (7.10)	19 (7.30)	-
No	16 (72.7)	216 (90.8)	232 (89.2)	-

4Ch = four chambers; DT = deceleration time; FW = free wall; GLS = global longitudinal strain; IVC = inferior vena cava; IVRT = isovolumetric relaxation time; IVS = interventricular septum; PW = posterior wall; LA = left atrium; LAs = left atrium strain; LLN = lower limit of normal; LV = left ventricle; LVEDD = left ventricle end-diastolic diameter; LVEDV = left ventricle end-diastolic volume; LVEF = left ventricle ejection fraction; LVESD = left ventricle end-systolic diameter; LVESV = left ventricle end-systolic volume; LVFP = left ventricle filling pressure; PASP = pulmonary artery systolic pressure; RA = right atrium; RV = right ventricle; SD = standard deviation; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

* Variable with a non-normal distribution. Values correspond to median [percentile 25 – percentile 75]. ** LLN according to age based on: Miyoshi T, Addetia K, Citro R, Daimon M, Desale S, Fajardo PG, et al. Left Ventricular Diastolic Function in Healthy Adult Individuals: Results of the World Alliance Societies of Echocardiography Normal Values Study. J Am Soc Echocardiogr 2020;33:1223–1233. doi: 10.1016/j.echo.2020.06.008.

*** LLN according to age based on table 3 of: Singh A, Carvalho Singulane C, Miyoshi T, Prado AD, Addetia K, Bellino M, et al. Normal Values of Left Atrial Size and Function and the Impact of Age: Results of the World Alliance Societies of Echocardiography Study. J Am Soc Echocardiogr 2022;35:154–164.e3. doi: 10.1016/j.echo.2021.08.008.

**** LLN based on table 1 of: Mukherjee M, Rudski LG, Addetia K, Afilalo J, D'Alto M, Freed BH, et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults and Special Considerations in Pulmonary Hypertension: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2025 Mar;38(3):141-186. doi: 10.1016/j.echo.2025.01.006.

***** Diastolic dysfunction according to the algorithms published in Robinson S, Ring L, Oxborough D, Harkness A, Bennett S, Rana B, et al. The assessment of left ventricular diastolic function: Guidance and recommendations from the British Society of Echocardiography. Echo Res Pract 2024;11:16. doi:10.1186/s44156-024-00051-2.

Table III. Primary and secondary outcomes across study groups.

	Low LAs – n (%)	Normal LAs – n (%)	Hazard ratio [95% CI]	p value
Primary outcome				
ACE	2 (9.10)	18 (7.60)	1.31 [0.31 – 5.66]	0.715
Secondary outcomes				
Cardiovascular death	0 (0.00)	3 (1.30)	-	-
HF hospitalization	1 (4.50)	7 (2.90)	1.65 [0.20 – 13.43]	0.639
Atrial fibrillation	1 (4.50)	3 (1.30)	3.91 [0.41 – 37.57]	0.238
All-cause mortality	2 (9.10)	11 (4.60)	2.12 [0.47 – 9.58]	0.327

ACE = adverse cardiovascular event (composite endpoint of cardiovascular death, heart failure hospitalization, atrial fibrillation, myocardial infarction, and stroke); CI = confidence interval; HF = heart failure; LAs = left atrium strain.

Table IV. Univariate Spearman correlations and partial correlations, controlling for age and sex, between LARs and clinical parameters, biomarkers, and echocardiographic values.

Variable	LARs			
	Pearson correlation coefficient (r)	p value	Partial correlation (r)	p value
Age (years)	-0.387	< 0.001	-	
DAS28-ESR	-0.041	0.539	-	
RA disease duration (years)	-0.163	0.008	-0.070	0.261
6MWT distance (m)	0.216	< 0.001	0.031	0.631
NT-ProBNP (pg/mL)	-0.248	< 0.001	-0.145	0.021
E/e' ratio	-0.303	< 0.001	-0.150	0.016
ESR (mm/s)	-0.183	0.004	0.092	0.149
LV GLS (%)	-0.304	< 0.001	-0.253	< 0.001
RV GLS (%)	-0.243	0.001	-0.216	0.004
TAPSE (mm)	0.134	0.031	0.139	0.026

6MWT = 6-minute walk test; DAS28-ESR = Disease Activity Score 28 using ESR; ESR = erythrocyte sedimentation rate; GLS = global longitudinal strain; LARs = left atrium reservoir strain; LV = left ventricle; NT-Pro-BNP = N-terminal pro-brain natriuretic peptide; RA = rheumatoid arthritis; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion.

Table V. Characterization of the studied subgroups according to RV strain.

General features	Low RVs (n = 34)	Normal RVs (n = 146)	Overall (n = 180)	p value
Age (years)	57.2 (± 10.5)	53.1 (± 14.0)	53.9 (± 13.5)	0.059
Sex (female)	21 (61.8)	126 (86.3)	147 (81.7)	**< 0.001**
BMI (Kg/m^2)	26.5 (± 4.38)	25.3 (± 4.11)	25.6 (± 4.18)	0.142
BSA (m^2) *	1.77 (± 0.19)	1.69 (± 0.18)	1.71 (± 0.18)	**0.027**
SBP (mmHg)	136 (± 17.7)	130 (± 19.9)	130 (± 19.6)	0.116
DBP (mmHg)	79.1 (± 10.8)	74.7 (± 10.3)	75.5 (± 10.5)	**0.027**
Heart rate (bpm)	82.1 (± 14.5)	77.0 (± 11.7)	77.9 (± 12.3)	**0.031**
Sinus rhythm	34 (100)	146 (100)	180 (100)	-
QRS duration (ms) *	92.0 [83.5 – 104]	90.0 [85.0 – 98.0]	90.0 [84.8 – 100]	0.401
6MWT distance (m) *	390 [360 – 460]	400 [355 – 450]	398 [360 – 450]	0.385
Comorbidities and cardiovascular risk factors				
History of stroke	0 (0.00)	2 (1.40)	2 (1.10)	1.000
COPD	1 (2.90)	4 (2.70)	5 (2.80)	1.000
Chronic kidney disease	1 (2.90)	2 (1.40)	3 (1.70)	0.468
Diabetes mellitus	5 (14.7)	13 (8.90)	18 (10.0)	0.341
Hypertension	17 (50.0)	51 (34.9)	68 (37.8)	0.103
Dyslipidemia	10 (29.4)	60 (41.1)	70 (38.9)	0.208
Obesity	5 (14.7)	19 (13.0)	24 (13.3)	0.782
Tobacco smoking	18 (52.9)	45 (30.8)	63 (35.0)	**0.015**
RA duration (years) *	7.60 [2.59 – 13.5]	6.64 [3.52 – 12.5]	6.68 [3.51 – 13.0]	0.689
DAS28-ESR	2.76 (± 1.02)	2.85 (± 1.20)	2.83 (± 1.17)	0.723
RA medication				
NSAIDs	12 (35.3)	45 (30.8)	57 (31.7)	0.614
Corticosteroids	15 (44.1)	60 (41.1)	75 (41.7)	0.748
Methotrexate	20 (58.8)	96 (65.8)	116 (64.4)	0.447
Biologics	5 (14.7)	25 (17.1)	30 (16.7)	0.733
Others	18 (52.9)	57 (39.0)	75 (41.7)	0.139
Chronic medication				
Insulin	3 (8.82)	8 (5.48)	11 (6.11)	1.000
OAD	4 (11.8)	10 (6.85)	14 (7.78)	1.000
ACEi/ARB	12 (35.3)	40 (27.4)	52 (28.9)	0.360
Beta-blocker	4 (11.8)	6 (4.10)	10 (5.60)	0.096
CCB	6 (17.6)	12 (8.20)	18 (10.0)	0.114
MRA	1 (2.90)	0 (0.00)	1 (0.60)	-
Thiazide diuretic	5 (14.7)	16 (11.0)	21 (11.7)	0.556
Loop diuretic	0 (0.00)	2 (0.00)	2 (1.10)	1.000
Statin	8 (23.5)	46 (31.5)	54 (30.0)	0.361
Laboratory serum parameters				
Hemoglobin (g/dL)	13.6 (± 1.06)	13.0 (± 1.37)	13.2 (± 1.33)	**0.030**
Leucocytes (x10^9/L)	7440 (± 1948)	6988 (± 2201)	7074 (± 2157)	0.272
Creatinine (mg/dL)	0.80 (± 0.20)	0.73 (± 0.15)	0.75 (± 0.16)	**0.026**

eGFR (ml/min/1.73m^2) **	89.2 (± 17.4)	95.2 (± 18.0)	94.3 (± 18.0)	**0.081**
HbA1c (%) *	5.59 [5.20 – 5.80]	5.48 [5.10 – 5.70]	5.40 [5.10 – 5.70]	0.120
Total cholesterol (mg/dL)	210 (± 40.1)	181 (± 32.6)	187 (± 36.0)	**< 0.001**
LDL cholesterol (mg/dL)	121 (± 31.2)	95.8 (± 28.5)	101 (± 30.6)	**< 0.001**
HDL cholesterol (mg/dL)	60.3 (± 16.4)	63.0 (± 16.5)	62.5 (± 16.4)	0.397
HsTnT (mg/mL) *	0.003 [0.002 – 0.005]	0.003 [0.002 – 0.006]	0.005 [0.002 – 0.005]	0.819
NT-ProBNP (pg/mL) *	54.9 [3078 – 96.6]	75.2 [44.1 – 139]	71.5 [40.2 – 122]	0.058
ESR (mm/h)	20.3 (± 13.7)	23.0 (± 16.8)	22.5 (± 16.3)	0.384
C-reactive protein (mg/L) *	3.89 [1.13 – 9.12]	7.88 [0.80 – 6.31]	2.50 [0.98 – 6.79]	0.087
Ferritin (ng/mL) *	108 [43.0 – 165]	96.0 [45.0 – 171]	97 [45.0 – 169]	0.474
Anti-CCP or rheumatoid factor (positive)	26 (76.5)	112 (76.7)	138 (76.7)	0.976

6MWT = 6 minute walk test; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; BSA = body surface area; CCB = calcium channel blocker; CCP = cyclic citrullinated peptides; COPD = chronic obstructive pulmonary disease; DAS28-ESR = Disease Activity Score 28 using ESR; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; ESR = erythrocyte sedimentation rate; HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; HsTnT = high-sensitivity troponin T; LDL = low-density lipoprotein; MRA = mineralocorticoid receptor antagonist; NSAIDs = non-steroidal anti-inflammatory drugs; OAD = oral anti-diabetic; NT-Pro-BNP = Nterminal pro-brain natriuretic peptide; RA = rheumatoid arthritis; RV = right ventricle; RVs = right ventricle strain; SBP = systolic blood pressure; SD = standard deviation.

Values correspond to mean (SD) or n (%) where appropriate.

Low right ventricle strain refers to low right ventricle global longitudinal strain or low right ventricle free wall strain base on the cut-offs reported on table 1 of: Mukherjee M, Rudski LG, Addetia K, Afilalo J, D'Alto M, Freed BH, et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults and Special Considerations in Pulmonary Hypertension: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2025 Mar;38(3):141-186. doi: 10.1016/j.echo.2025.01.006.

* Variable with a non-normal distribution. Values correspond to median [percentile 25 – percentile 75]. ** eGFR using the CKD-EPI formula: Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. N Engl J Med 2021;385:1737–1749. doi:10.1056/NEJMoa2102953.

Table VI. Echocardiographic parameters according to RV strain groups.

	Low RVs (n = 34)	Normal RVs (n = 146)	Overall (n = 180)	p value
Aortic stenosis				
Mild	5 (14.7)	10 (7.00)	15 (8.50)	-
Moderate	4 (2.80)	0 (0.00)	4 (2.30)	-
Aortic regurgitation				
Mild	0 (0.00)	7 (4.90)	7 (3.90)	-
Moderate	0 (0.00)	2 (1.40)	2 (1.10)	-
Mitral stenosis				
Mild	0 (0.00)	1 (0.70)	1 (0.60)	-
Mitral regurgitation				
Mild	11 (33.3)	55 (37.9)	66 (37.1)	-
Moderate	0 (0.00)	3 (2.10)	3 (1.70)	-
Pericardial effusion	0 (0.00)	1 (0.70)	1 (0.60)	-
IVC diameter (mm)	15.3 (± 2.64)	15.7 (± 2.77)	15.6 (± 2.74)	0.525
IVS thickness (mm)	8.62 (± 1.92)	8.21 (± 1.93)	8.29 (± 1.93)	0.271
PW thickness (mm)	8.09 (± 1.67)	7.66 (± 1.57)	7.74 (± 1.59)	0.162
LV mass indexed (g/m^2)	67.1 (± 17.8)	63.1 (± 18.2)	63.9 (± 18.1)	0.247
LVEDD (mm)	44.6 (± 4.75)	43.4 (± 5.08)	43.7 (± 5.03)	0.219
LVESD (mm)	29.3 (± 11.1)	28.4 (± 4.65)	28.6 (± 6.37)	0.669
LVEDV indexed (mL/m^2)	46.2 (± 11.7)	49.8 (± 12.4)	49.1 (± 12.3)	0.121
LVESV indexed (mL/m^2)	18.1 (± 5.33)	18.3 (± 5.22)	18.2 (± 5.23)	0.817
Stroke volume indexed (mL/m^2)	40.9 (± 9.68)	40.1 (± 10.8)	40.2 (± 10.6)	0.648
Cardiac output (L/min)	5.04 (± 1.38)	4.83 (± 1.33)	4.87 (± 1.34)	0.718
LVEF (%)	61.2 (± 6.01)	62.5 (± 5.90)	62.3 (± 5.93)	0.242
LA area (cm^2)	18.2 (± 3.64)	18.4 (± 3.83)	18.4 (± 3.79)	0.655
LA volume indexed (mL/m^2)	30.5 (± 7.55)	32.5 (± 9.93)	31.8 (± 9.54)	0.376
RA area (cm^2)	13.9 (± 2.81)	13.9 (± 2.95)	13.9 (± 2.91)	0.917
RV basal diameter (mm) *	30.0 [20.0 – 37.5]	30.0 [23.0 – 38.0]	30.0 [22.0 – 38.0]	0.711
Mitral E wave (cm/s)	70.1 (± 16.6)	75.9 (± 17.0)	74.8 (± 17.0)	0.054
Mitral E/A ratio *	0.90 [0.76 – 1.10]	1.00 [0.84 – 1.30]	1.00 [0.83 – 1.30]	0.087
Mitral E wave DT (ms)	150 (± 43.5)	151 (± 41.6)	151 (± 41.8)	0.683
Ar-A duration (ms)	0.81 (± 28.7)	-12.1 (± 24.5)	-9.56 (± 25.8)	**0.011**
IVRT (ms)	92.5 (± 21.8)	87.9 (± 17.6)	88.8 (± 18.5)	0.186
e' septal (cm/s)	6.79 (± 1.49)	8.36 (± 2.57)	8.06 (± 2.48)	**< 0.001**
e' lateral (cm/s)	10.3 (± 2.53)	11.7 (± 3.39)	11.4 (± 3.28)	**0.008**
E/e' average *	8.70 [7.04 – 10.1]	8.00 [6.60 – 9.50]	8.10 [6.70 – 9.73]	0.171
e' < LLN for age **	4 (11.8)	8 (5.50)	12 (6.70)	0.246
S' tricuspid annulus (cm/s)	13.3 (± 2.45)	14.2 (± 2.90)	14.1 (± 2.84)	0.090
TAPSE (mm) *	23.5 [20.0 – 26.0]	24.0 [22.0 – 27.0]	24.0 [21.0 – 26.0]	0.074
TR maximum velocity (m/s)	2.30 (± 0.25)	2.19 (± 0.33)	2.21 (± 0.32)	0.211
PASP (mmHg) *	22.0 [20.5 – 25.5]	22.0 [18.0 – 26.0]	22.0 [19.0 – 25.8]	0.922
LV GLS (%)	-19.1 (± 2.34)	-21.3 (± 2.44)	-20.9 (± 2.57)	**< 0.001**

Normal Borderline	19 (57.6) 14 (42.4)	129 (93.5) 9 (6.50)	148 (86.5) 23 (13.5)	**< 0.001**
LA reservoir strain	35.6 (± 9.19)	38.7 (± 10.1)	38.1 (± 10.0)	0.104
Low (according to age) ***	1 (2.90)	4 (2.70)	5 (2.80)	1.000
LA conduit strain	-17.7 (± 8.09)	-22.1 (± 9.62)	-21.3 (± 9.49)	**0.015**
LA pump strain	-17.9 (± 6.13)	-16.5 (± 7.01)	-16.8 (± 6.85)	0.308
Low (according to age) ***	2 (5.90)	7 (4.80)	9 (5.00)	0.679
FW RV strain	-17.5 (± 3.04)	-28.5 (± 4.62)	-26.4 (± 6.15)	**< 0.001**
RV GLS	- 15.2 (± 2.21)	- 23.7 (± 3.32)	- 22.1 (± 4.58)	**< 0.001**
Diastolic dysfunction (2024) ****				
Yes, with elevated LVFP	1 (2.90)	6 (4.10)	7 (3.90)	-
Yes, with normal LVFP	4 (11.8)	7 (4.80)	11 (6.10)	-
No	29 (85.3)	133 (91.1)	162 (90.0)	-

4Ch = four chambers; DT = deceleration time; FW = free wall; GLS = global longitudinal strain; IVC = inferior vena cava; IVRT = isovolumetric relaxation time; IVS = interventricular septum; PW = posterior wall; LA = left atrium; LAs = left atrium strain; LLN = lower limit of normal; LV = left ventricle; LVEDD = left ventricle end-diastolic diameter; LVEDV = left ventricle end-diastolic volume; LVEF = left ventricle ejection fraction; LVESD = left ventricle end-systolic diameter; LVESV = left ventricle end-systolic volume; LVFP = left ventricle filling pressure; PASP = pulmonary artery systolic pressure; RA = right atrium; RV = right ventricle; SD = standard deviation; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

* Variable with a non-normal distribution. Values correspond to median [percentile 25 – percentile 75]. ** LLN according to age based on: Miyoshi T, Addetia K, Citro R, Daimon M, Desale S, Fajardo PG, et al. Left Ventricular Diastolic Function in Healthy Adult Individuals: Results of the World Alliance Societies of Echocardiography Normal Values Study. J Am Soc Echocardiogr 2020;33:1223–1233. doi: 10.1016/j.echo.2020.06.008.

*** LLN according to age based on: Singh A, Carvalho Singulane C, Miyoshi T, Prado AD, Addetia K, Bellino M, et al. Normal Values of Left Atrial Size and Function and the Impact of Age: Results of the World Alliance Societies of Echocardiography Study. J Am Soc Echocardiogr 2022;35:154–164.e3. doi: 10.1016/j.echo.2021.08.008.

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Table VII. Primary and secondary outcomes across study groups.

	Low RVs – n (%)	Normal RVs – n (%)	Hazard ratio [95% CI]	p value
Primary outcome				
ACE	4 (11.8)	8 (5.50)	2.28 [0.685 – 7.56]	0.179
Secondary outcomes				
Cardiovascular death	1 (2.90)	1 (0.70)	4.43 [0.28 – 70.8]	0.293
HF hospitalization	2 (5.90)	4 (2.70)	2.21 [0.41 – 12.1]	0.359
Atrial fibrillation	1 (2.90)	0 (0.00)	-	-
All-cause mortality	2 (5.90)	5 (3.40)	1.76 [0.34 – 9.07]	0.500

ACE = adverse cardiovascular event (composite endpoint of cardiovascular death, heart failure hospitalization, atrial fibrillation, myocardial infarction, and stroke); CI = confidence interval; HF = heart failure; LAs = left atrium strain.

Table VIII. Univariate Spearman correlations and partial correlations, controlling for age and sex, between RV GLS and clinical parameters, biomarkers, and echocardiographic values.

Variable	RV GLS			
	Pearson correlation coefficient (r)	p value	Partial correlation (r)	p value
Age (years)	0.169	0.023	-	-
DAS28-ESR	-0.013	0.875	-	-
RA disease duration (years)	0.091	0.227	-	-
6MWT distance (m)	-0.010	0.894	-	-
NT-ProBNP (pg/mL)	-0.129	0.089	-	-
Serum creatinine (mg/dL)	0.115	0.125	-	-
C-reactive protein (mg/L)	0.028	0.717	-	-
e' septal	-0.302	< 0.001	-0.245	0.001
LV GLS (%)	0.396	< 0.001	0.329	< 0.001
LARs (%)	-0.243	0.001	-0.216	0.004
S' tricuspid annulus (cm/s)	-0.173	0.023	-0.210	0.006
TAPSE (mm)	-0.200	0.007	-0.215	0.004

6MWT = 6-minute walk test; DAS28-ESR = Disease Activity Score 28 using ESR; ESR = erythrocyte sedimentation rate; FWRVs = free wall right ventricle strain; GLS = global longitudinal strain; LARs = left atrium reservoir strain; LV = left ventricle; NT-Pro-BNP = N-terminal pro-brain natriuretic peptide; RA = rheumatoid arthritis; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion.

Figures

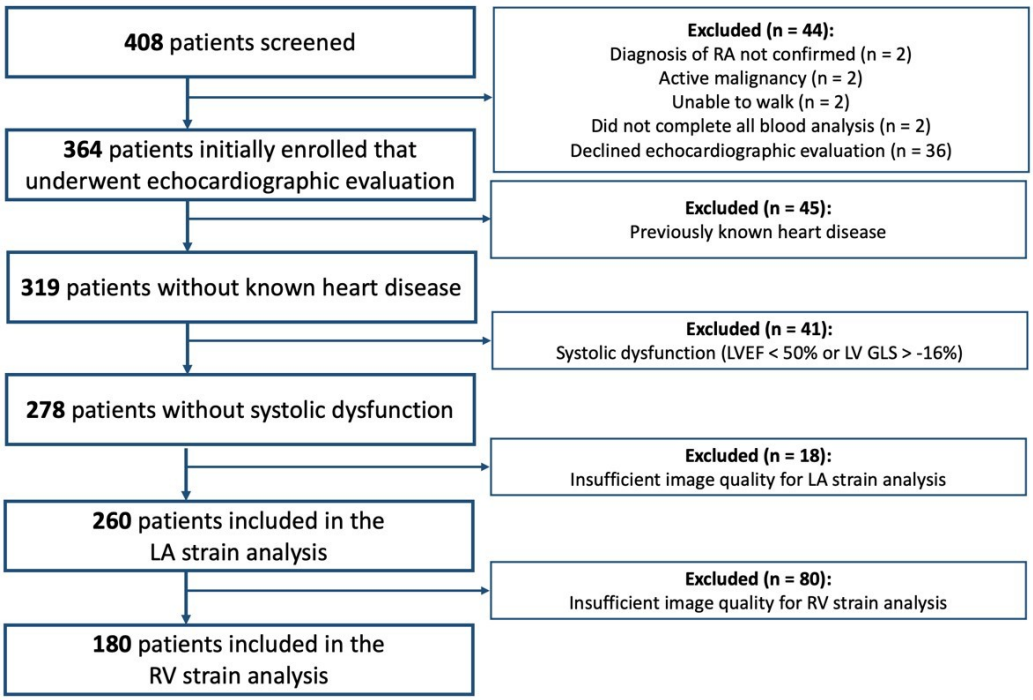

Figure 1 - Study population flow chart.

GLS = GLS = global longitudinal strain; LA = left atrium; LV = left ventricle; LVEF = left ventricle ejection fraction; RA = rheumatoid arthritis; RV = right ventricle

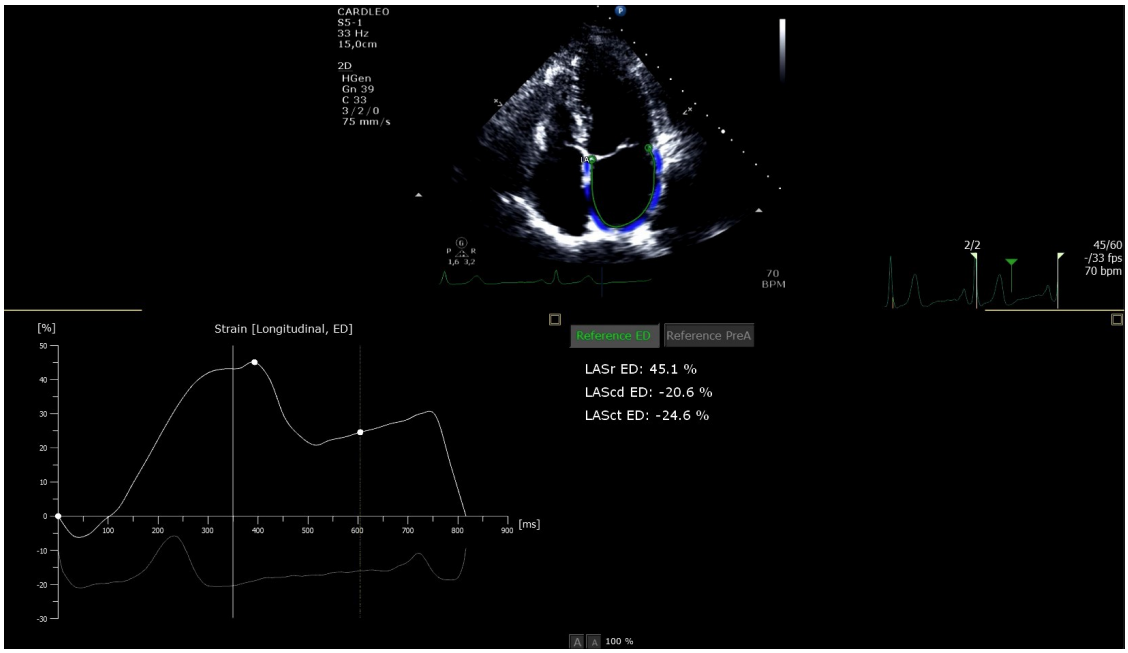

Figure 2 - Left Atrial Strain Curve (TomTec ®) and Regional Tracking Derived from Speckle-Tracking Imaging. IntelliSpace Cardiovascular, Philips Medical Systems.

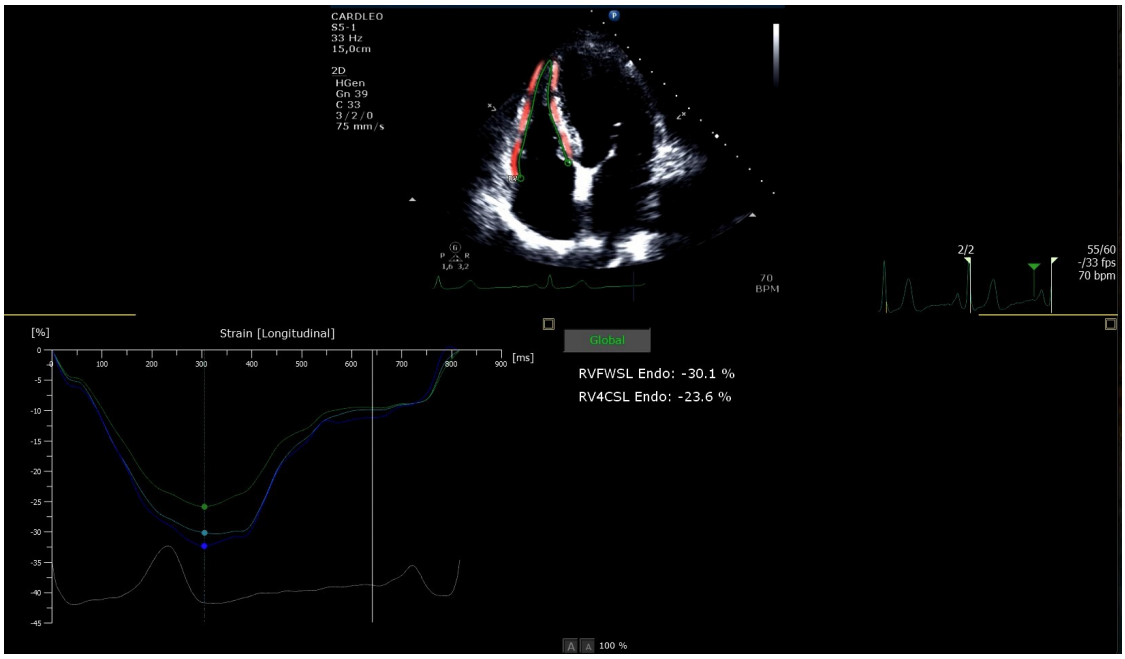

Figure 3 - Right Ventricle Strain Curve (TomTec ®) and Regional Tracking Derived from Speckle-Tracking Imaging. IntelliSpace Cardiovascular, Philips Medical Systems.

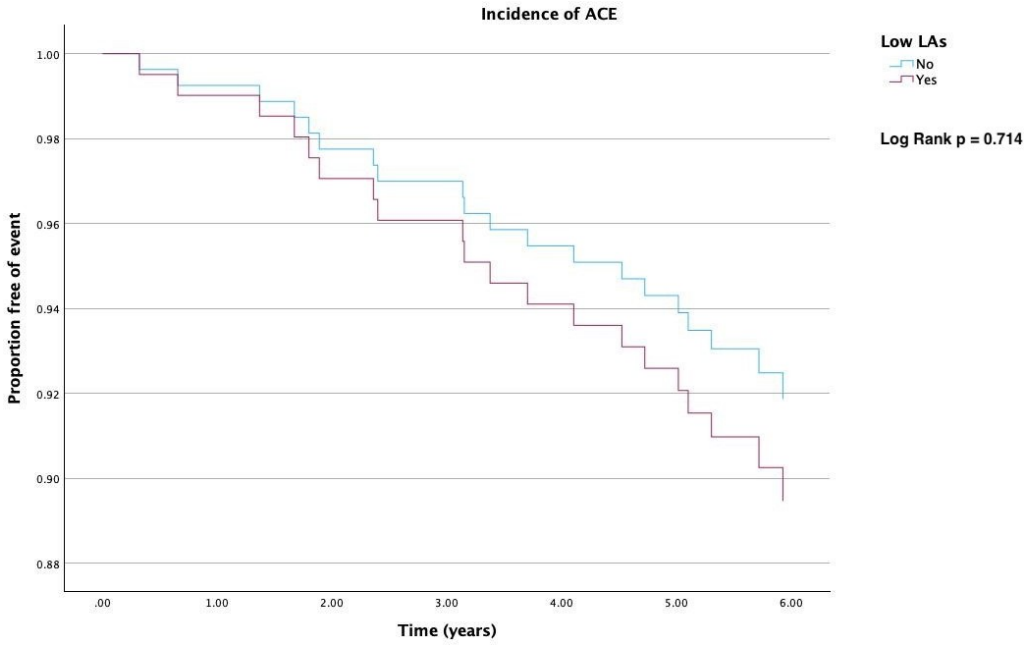

Figure 4 - Survival plot representing the incidence of the primary endpoint between the groups with low LAs and normal LAs.

ACE: adverse cardiovascular events; LAs left atrium strain

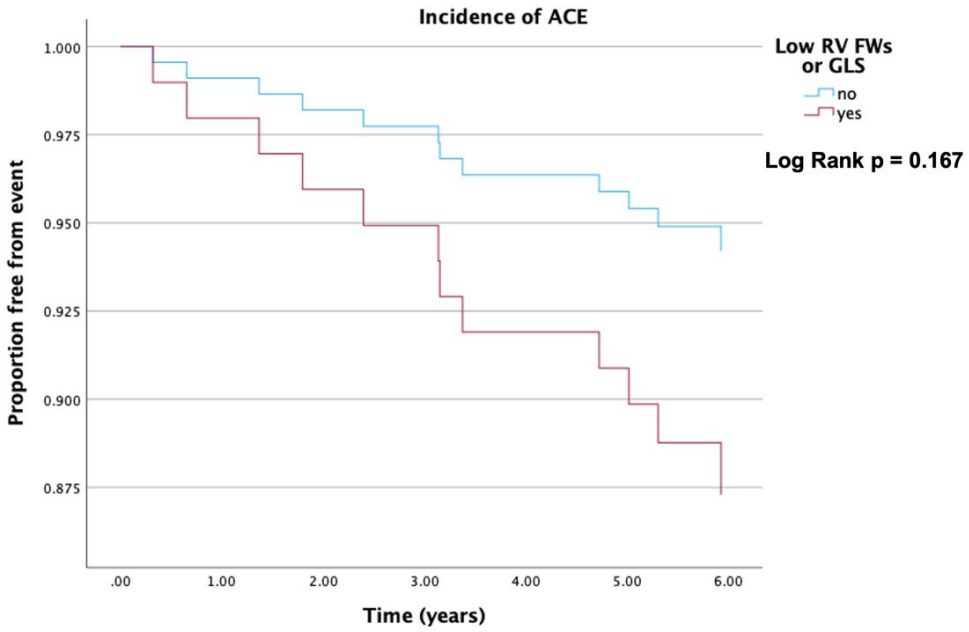

Figure 5 - Survival plot representing the incidence of the primary endpoint between the groups with low RV strain and normal RV strain.

ACE: adverse cardiovascular events; FWs: free wall strain; GLS: global longitudinal strain; RV: right ventricle.

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