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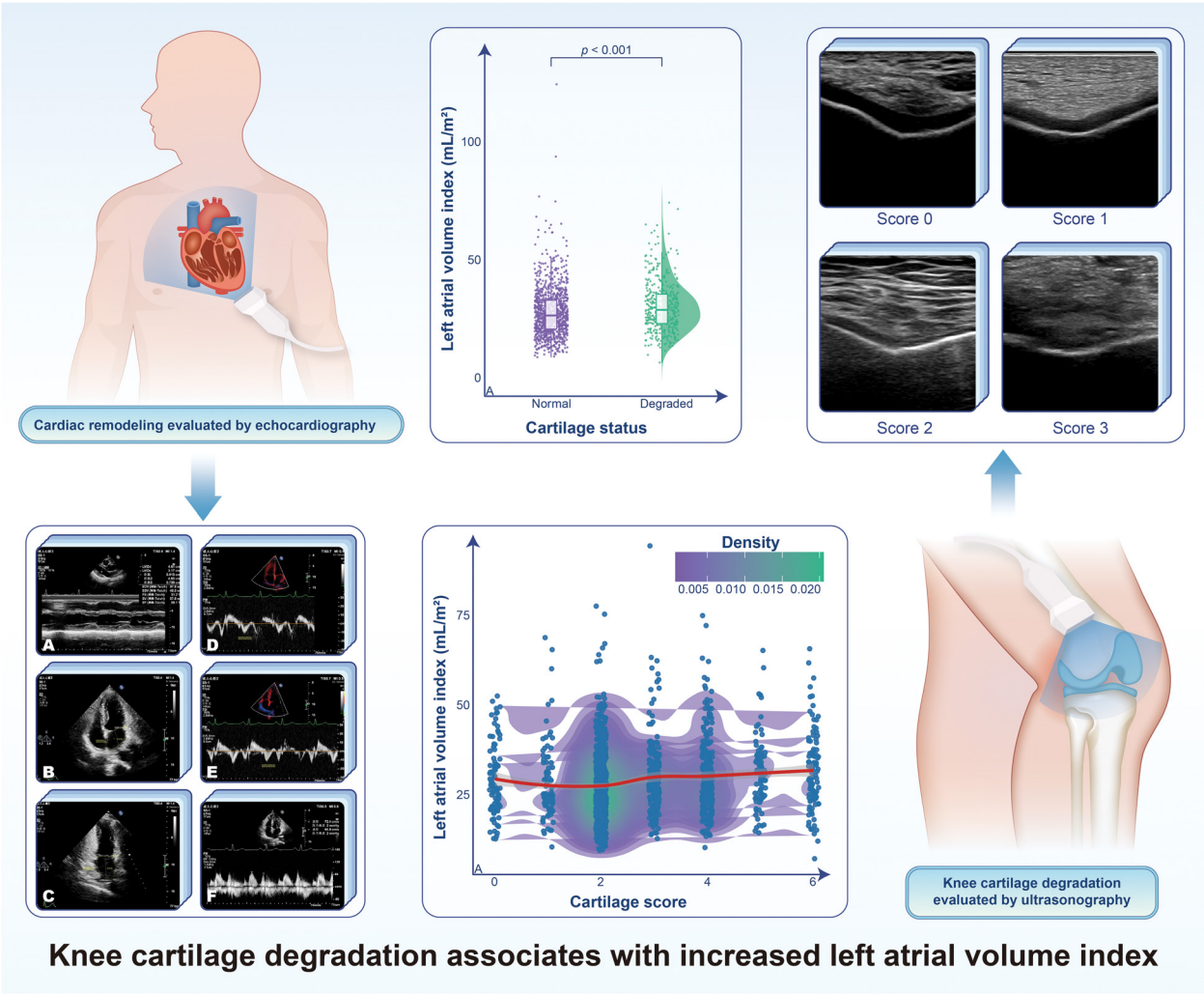
Association between knee cartilage degradation and cardiac remodeling

A cross-sectional analysis in a community-based cohort

Haoran Wang, MD[a,*], Qichao Wang, BSc[b], Bing He, MSc[a], Jing Bai, MSc[a], Nan Wang, MSc[a], Dongliang Liu, BSc[a], Jin Wang, MSc[a], Qiaotao Xie, MSc[a]

Graphical abstract



HW and QW contributed to this article equally.

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[a] Department of Cardiology, Cardiovascular Institute of Luohe, Luohe Central Hospital, Luohe Medical College, Luohe, China, [b] Department of Orthopedics, The Second Affiliated Hospital of Luohe Medical College, Luohe, China.

* Correspondence: Haoran Wang, Cardiovascular Institute of Luohe, Luohe Central Hospital, Luohe Medical College, Luohe 462000, Henan, China (e-mail: washingtonhr@163.com).

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Abstract

Objectives: Osteoarthritis, a leading cause of disability, has been epidemiologically linked to cardiovascular disease (CVD), yet the relationship between structural cartilage degeneration and cardiac remodeling remains poorly characterized. This cross-sectional study investigates whether knee cartilage degradation, quantified via ultrasonography, correlates with echocardiographic markers of subclinical cardiovascular dysfunction.

Methods: Middle-aged and elderly people aged 35 to 75 years who met the inclusion criteria were enrolled. Knee cartilage degradation was scored (0–3 per side) using ultrasound, with total scores categorized as normal (0–3, $n = 1{,}041$) or degraded (≥ 4, $n = 430$). Cardiac structure and function parameters, including left ventricular ejection fraction, left atrial volume index (LAVI), left ventricular mass index, and diastolic function (mitral valve *e*' and *E*/*e*' ratio), were measured by echocardiography. Group comparison, logistic regression, subgroup and sensitivity analyses, and XGBoost machine learning were used to assess associations and feature importance.

Results: Participants with degraded cartilage were older (median age 64 vs. 58 years, $p < 0.001$) and had a lower male proportion (31% vs. 45%, $p < 0.001$). The degraded group exhibited a significantly higher median LAVI (29 vs. 27 mL/m², $p < 0.001$). Subgroup and sensitivity analyses confirmed that the association with LAVI was robust. XGBoost analysis identified cartilage degradation as an important contributor to LAVI (standardized gain value 4.89%, ranking 10th among 24 variables).

Conclusions: Knee cartilage degeneration is associated with left atrial enlargement. These findings underscore the potential role of osteoarthritis-related structural joint damage in subclinical cardiac remodeling, offering a foundation for future exploration of comprehensive care strategies.

Abbreviations: AF = atrial fibrillation, CVD = cardiovascular disease, CHD = coronary heart disease, HF = heart failure, IRB = institutional review board, IQR = interquartile range, LAVI = left atrial volume index, LVEF = left ventricular ejection fraction, LVMI = left ventricular mass index, MS = metabolic syndrome, OA = osteoarthritis.

Keywords: cardiac remodeling, knee cartilage degeneration, left atrial volume index, osteoarthritis, population study

1. Introduction

Osteoarthritis (OA), affecting over a quarter of adults ≥ 40 years, is a leading cause of disability, with knee OA characterized by articular cartilage degeneration.[1,2] While traditionally viewed as a local degenerative disease, OA is now recognized as a systemic disorder involving inflammation, metabolic dysfunction, and mechanical stress-pathways overlapping with cardiovascular diseases (CVDs), the global leading cause of mortality.[3–8] Epidemiological links between OA and CVD exist,[9] yet how objective measures of cartilage degeneration relate to cardiac structure/function remain unclear.

Prior studies relied on radiographic OA severity or self-reported pain, failing to capture cartilage degradation.[10–15] No human research has directly associated cartilage damage with echocardiographic markers like left atrial volume index (LAVI), left ventricular mass index (LVMI), or diastolic function (mitral *e*' velocity, *E*/*e*' ratio). This gap is critical: early cardiac remodeling (e.g., atrial enlargement, diastolic dysfunction) predicts adverse outcomes but is often undetected, making cartilage-cardiac associations pivotal for risk prediction.

We hypothesize that knee cartilage degeneration, scored via ultrasound, correlates with adverse cardiac changes: increased LAVI (atrial remodeling), altered LVMI (ventricular hypertrophy), and reduced diastolic function (lower *e*' velocity, higher *E*/*e*' ratio). These relationships may reflect shared mechanisms: cartilage degeneration related pain-induced inactivity exacerbates cardiovascular deconditioning.

Using a community-based cohort, this cross-sectional study aims to assess associations between objective cartilage degeneration and cardiac parameters. By focusing on precise cartilage and cardiac measurements, the study addresses a key limitation of prior research, which conflated OA symptoms with cardiovascular risk. Ultrasound for the assessment of knee cartilage has been proved to be efficient, systematic, and reliable.[16,17] Findings may establish cartilage degeneration as a novel biomarker for subclinical cardiac remodeling, informing integrated care for patients with structural joint damage. This work advances the understanding of OA as a systemic disease, bridging localized cartilage damage with cardiovascular health and offering a foundation for future longitudinal studies.

2. Methods

2.1. Research population recruitment

This cross-sectional study utilized data from a cohort established in Luohe city and its surrounding areas—The Longitudinal Investigation of Osteoarthritis and Cardiovascular Health Status cohort. The target population consisted of middle-aged and elderly individuals aged between 35 and 75 years. The selection of this age range was based on the high prevalence of knee cartilage degeneration and CVDs within this demographic group. The inclusion criteria were as follows: residing permanently in Luohe city and its surrounding areas, ensuring long-term follow-up feasibility; willingness and ability to undergo relevant cardiac ultrasound, carotid ultrasound, and

X-ray and ultrasound imaging of the shoulder, knee, and hip joints for the assessment of CVDs and OA; and willingness and capacity to participate in a follow-up period of at least 5 years (although this cross-sectional analysis is based on baseline data, the long-term follow-up plan was part of the original cohort design).

The exclusion criteria were as follows: patients in the acute phase of acute myocardial infarction, with cardiogenic shock, or at the end-stage of heart failure (HF), as well as those with hemodynamic instability due to other causes; patients with a confirmed diagnosis of malignant tumors, severe trauma (such as severe burns and car accidents) that endangered life or significantly affected life expectancy; and patients with severe mental and psychological abnormalities, impaired consciousness, or cognitive impairment, who were unable to cooperate with the questionnaire survey, to ensure the accuracy and reliability of the collected data.

All potential participants were provided with detailed information about the study, including its procedures, potential risks, and benefits. Informed consent was obtained from each participant after they fully understood the study details. The informed consent process was conducted in a face-to-face manner by trained research staff, and participants were given sufficient time to ask questions and make decisions.

The sample size was based on an anticipated 40% possibility of cardiovascular events in the study population. The confidence interval was set to be 95%, with an assumed relative risk of 1.2 according to previous studies. When the statistical power was set to be over 80%, we needed a total sample size of 1,202. To allow for a potential 20% rate of follow-up loss, the required sample size was increased to 1,500. From November 2023 to November 2024, a total of 1,762 study participants who met the inclusion and exclusion criteria were initially enrolled in the cohort. Among them, 119 and 172 participants did not undergo knee ultrasonographic/echocardiographic assessment, respectively. After excluding these individuals, the baseline information of the remaining 1,471 participants was incorporated into the statistical analysis for the cross-sectional study.

2.2. Clinical data acquisition and measurement

2.2.1. Knee cartilage evaluation. The assessment of knee cartilage was a crucial part of this study. Knee cartilage was quantitatively evaluated using a specific method. The cartilage in the intercondylar fossa was scored from 0 to 3 points. This scoring system was based on an established cartilage assessment criteria.[18,19] Briefly, a score of 0 represented a monotonous anechoic band having a sharp hyperechoic anterior and posterior interface. A score of 1 indicated loss of the normal sharpness of cartilage interfaces and/or increased echogenicity of the cartilage. A score of 2 corresponded to clear local thinning of the cartilage. A score of 3 denoted severe cartilage damage, characterized by significant cartilage loss. The original DICOM image files (exported from Philips Epic-5 or Esaote Class-C that we used) of cartilage and cardiac ultrasound imaging were anonymized and then archived separately, and the cartilage ultrasound images were evaluated by 2 researchers. The scores of the bilateral intercondylar fossa cartilages were added together. For cartilage ultrasound (n = 100 images), intrarater kappa values were 0.849 and 0.896, and interobserver kappa was 0.819, indicating excellent agreement.

2.2.2. Cardiac structure and function measurement. The cardiac parameters indices we selected are all based on the recommendations of the Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2024,[20] which include the following indices:

Left ventricular ejection fraction: Left ventricular ejection fraction (LVEF) was calculated using M-mode echocardiography with the Teichholz formula: $\mathrm{LVEF} = \left(1 - \frac{\mathrm{LVIDs}^3}{\mathrm{LVIDd}^3}\right) * 100\%$, where LVIDs and LVIDd represent the internal diameter of left ventricular at the phase of end-systole and end-diastole, respectively.

LAVI (mL/m^2): LAVI could be computed using the area-length approximation: $\frac{8}{3\pi}\left[\frac{(\mathrm{A1}*\mathrm{A2})}{L}\right]$, where A1 and A2 are the corresponding LA areas, and the LA length (L) was defined as the shortest distance from the center of the mitral annulus measured in the apical 2- and 4-chamber views. The left atrial volume was then indexed to body surface area to account for differences in body size. An enlarged left atrium is associated with various cardiovascular conditions, including atrial fibrillation (AF), HF, and increased cardiovascular risk.[21]

LVMI (g/m^2): LVMI was calculated using the formula: $\mathrm{LV\ mass} = 0.8 * 1.04 * \left[(\mathrm{IVS} + \mathrm{LVID} + \mathrm{PWT})^3 - \mathrm{LVID}^3\right] + 0.6g,$ where IVS is interventricular septum; LVID is LV internal diameter, and PWT is posterior wall thickness. LVMI was then indexed to body surface area. Left ventricular hypertrophy is a significant risk factor for cardiovascular morbidity and mortality.[21]

Mitral valve *e*' (cm/s) and *E*/*e*' Ratio: In the apical 4-chamber view, use tissue Doppler imaging to place the sample volume at the lateral and septal insertion points of the mitral valve annulus, respectively, and measure the peak velocity of the e' wave at each site. Then, in the same view, switch to pulsed-wave Doppler mode, place the sample volume at the tips of the mitral valve leaflets to measure the peak velocity of the E wave. Finally, calculate the *E*/*e*' Ratio as the average of the values obtained by dividing the peak velocity of the E wave by the peak velocity of the e' wave measured at the lateral and septal walls.[22]

All the measurement of cardiac ultrasound followed clinical quality control standards. Based on the recommended criteria we classified whether there were abnormalities in cardiac structure and function including left

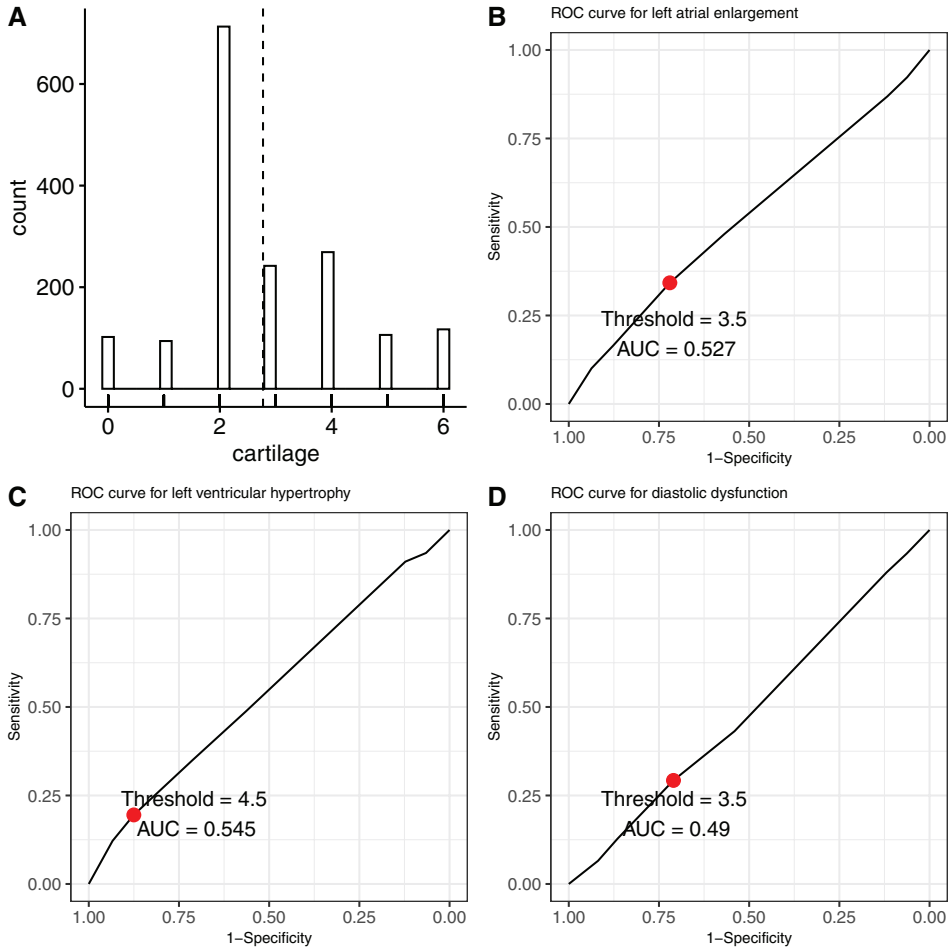

Figure 1. The distribution of cartilage degradation score in the study population (A), and the ROC curve [(B) for left atrial enlargement, (C) for left ventricular hypertrophy, and (D) for diastolic dysfunction] to generate the cutoff point for cartilage score. ROC = receiver operating characteristic.

atrial enlargement with LAVI > 33 mL/m^2 in males and >37 mL/m^2 in females, left ventricular hypertrophy with LVMI >109 g/m^2 in males and > 105 g/m^2 in females or relative wall thickness > 0.51, and diastolic dysfunction with the ratio of early mitral inflow velocity to early diastolic tissue Doppler mitral annulus velocity (*E*/*e*') >14, interventricular septal *e*' < 7 cm/s and left ventricular free wall *e*' < 10 cm/s.

2.2.3. Other clinical data collection. In addition to knee cartilage and cardiac parameters, a comprehensive set of other clinical data was collected from each participant. This included age, gender, smoking status (classified as current smoker or not), alcohol use (classified as yes or no), medical history data, including the presence of hypertension, diabetes, metabolic syndrome (MS), coronary heart disease (CHD), stroke, HF, and AF were obtained through self-report and confirmed by medical records when possible. Anthropometric measurements, such as height, weight, waist circumference, and body mass index, were taken using standardized procedures. Blood pressure was measured in the sitting position using a calibrated sphygmomanometer, and the average of 2 consecutive measurements was recorded. Blood samples were collected in the morning after at least 8 hours of fasting to measure lipid profiles, including total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides, as well as blood glucose levels. Besides, we also assessed the health-related quality of life by an EQ-5D-3L questionnaire, which could assess the mobility, self-care, daily-activity, pain, and depression status that related to both OA and CVD.

2.2.4. Statistical analysis. All statistical analyses were conducted using the R (version 4.4.2) statistical software. All p values are 2-tailed, and $p < 0.05$ was considered significant. Continuous variables were presented as median (25^{th}, 75^{th} percentile) due to their nonnormal distribution, while categorical variables were presented as counts (%).

The cutoff value for cartilage degradation was determined using receiver operating characteristic curve analysis for cardiac parameters (left atrial enlargement, left ventricular hypertrophy, and diastolic dysfunction) to categorize cartilage score into binary outcomes (normal/degraded). Differences in baseline characteristics between the "Normal" and "Degraded" cartilage groups

Table 1

Baseline characteristics of the study population by cartilage degradation classification.

Variable	Overall *N* = 1471	Normal *N* = 1041	Degraded *N* = 430	*p*-value
Age (years)	59 (53, 67)	58 (52, 67)	64 (56, 69)	9.44E-11
Gender (male)	602 (41%)	467 (45%)	135 (31%)	1.67E-06
Current smoking	321 (22%)	251 (24%)	70 (16%)	0.001
Alcohol use	135 (9.2%)	107 (10%)	28 (6.5%)	0.029
Hypertension	582 (40%)	395 (38%)	187 (43%)	0.055
Diabetes	129 (8.8%)	80 (7.7%)	49 (11%)	0.029
Coronary heart disease	97 (6.6%)	66 (6.3%)	31 (7.2%)	0.62
Stroke	165 (11%)	106 (10%)	59 (14%)	0.062
Metabolic syndrome	498 (34%) [5]	338 (33%) [5]	160 (37%)	0.104
Heart failure	22 (1.1%)	15 (1.2%)	7 (0.9%)	0.974
Atrial fibrillation	19 (1.3%)	15 (1.5%)	4 (0.9%)	0.814
Total cholesterol (mmol/L)	5.21 (4.22, 6.43) [3]	5.17 (4.22, 6.40) [2]	5.28 (4.24, 6.46) [1]	0.356
Low-density lipoprotein cholesterol (mmol/L)	2.97 (2.19, 4.16) [45]	2.95 (2.19, 4.17) [39]	3.00 (2.23, 4.11) [6]	0.799
High-density lipoprotein cholesterol (mmol/L)	1.39 (1.20, 1.62) [4]	1.38 (1.19, 1.62) [4]	1.41 (1.22, 1.61)	0.244
Triglycerides (mmol/L)	1.64 (1.15, 2.30) [1]	1.62 (1.14, 2.31) [1]	1.69 (1.21, 2.30)	0.198
Glucose (mmol/L)	5.60 (5.30, 6.30)	5.60 (5.30, 6.30)	5.70 (5.30, 6.40)	0.054
Systolic blood pressure (mmHg)	151 (137, 163)	151 (136, 163)	152 (140, 163)	0.095
Diastolic blood pressure (mmHg)	91 (81, 101)	91 (81, 101)	90 (81, 101)	0.839
Waist circumference (cm)	88 (81, 95)	88 (81, 95)	89 (82, 96)	0.422
Body mass index (kg/m^2)	25.8 (23.6, 28.1) [3]	25.7 (23.6, 28.0) [3]	25.9 (23.6, 28.5)	0.309
Mitral valve E velocity (M/S)	8.31 (6.85, 10.04) [2]	8.31 (6.84, 10.08) [2]	8.31 (6.87, 9.95)	0.631
Left atrial volume index (mL/m^2)	27 (21, 34) [3]	27 (21, 33) [2]	29 (23, 36) [1]	1.27E-05
Left ventricular mass index (g/m^2)	77 (67, 89) [1]	78 (67, 89) [1]	77 (66, 91)	0.956
Relative wall thickness	0.38 (0.34, 0.42)	0.38 (0.34, 0.41)	0.38 (0.34, 0.42)	0.051
Mitral valve *E*/*e*' (ratio)	8.13 (6.33, 10.17) [8]	8.10 (6.32, 10.06) [6]	8.27 (6.35, 10.31) [2]	0.579
Mitral valve septal *e*' velocity (m/s)	6.93 (5.59, 8.88) [2]	6.91 (5.61, 8.77) [2]	6.99 (5.47, 9.10)	0.711
Mitral valve lateral *e*' velocity (m/s)	9.5 (7.5, 11.6)	9.4 (7.5, 11.7)	9.5 (7.5, 11.4)	0.295
Left ventricular ejection fraction (%)	68 (63, 72)	68 (63, 71)	68 (64, 72)	0.478

This table presents the baseline characteristics of the study population, stratified by cartilage degradation classification (normal vs. degraded). Continuous variables are presented as median (25th, 75th percentile) [missing number], and categorical variables are presented as counts (%). *p*-values are from nonparametric tests for continuous variables and chi-square tests for categorical variables.
IVS = interventricular septum; RWT = relative wall thickness.

were compared, using nonparametric tests for continuous variables (the Wilcoxon rank-sum test) and chi-square tests for categorical variables. To explore the impact of knee cartilage degeneration on cardiac parameters, we first use raincloud plots to compare the difference between the "Normal" and "Degraded" cartilage groups. Scatter plots with density map and loess line was used to illustrate the distribution of cartilage score and cardiac parameters. Logistic regression was used to evaluate the association between cartilage degradation and cardiac abnormality (left atrial enlargement, left ventricular hypertrophy and diastolic dysfunction), and was illustrated by forest plots incorperating subgroup analyses by age groups, sex, smoking status, alcohol use, and medical history data (hypertension, diabetes, MS, CHD, stroke, HF, and AF). Besides, we performed sensitivity analysis by excluding those with history of CVD (CHD, stroke, HF, and AF).

Additionally, considering the need to incorporate numerous confounder variables, the skewed distribution of variables, the potential collinearity and interaction effects among variables, and the fact that simply categorizing continuous variables into binary variables is unfavorable for quantitative evaluation, we decided to employ machine learning based on the XGBoost algorithm, and use the gain value to decide the importance of the cartilage degradation score in explaining the cardiac remodeling parameters. The accumulated gain value of over 90% was used as the cutoff value to chose the most important variables.

2.2.5. Ethical considerations. This study was conducted in strict accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the institutional review board (IRB) of Luohe Central Hospital on April 13th, 2023 (approval number 2023010). The IRB carefully reviewed the study design, informed consent process, data collection methods, and potential risks and benefits to ensure the protection of participants' rights, safety, and well-being. The study was also registered on the Chinese Clinical Trial Registry (ChiCTR2300071492).

Informed consent was obtained from all participants before any study-related procedures were performed. The informed consent form provided detailed information about the study, including its purpose, procedures, potential risks (such as minimal discomfort during imaging procedures), and benefits (such as contributing to scientific knowledge and potentially improving future healthcare). Participants were informed that they had the right to withdraw from the study at any time without any negative consequences.

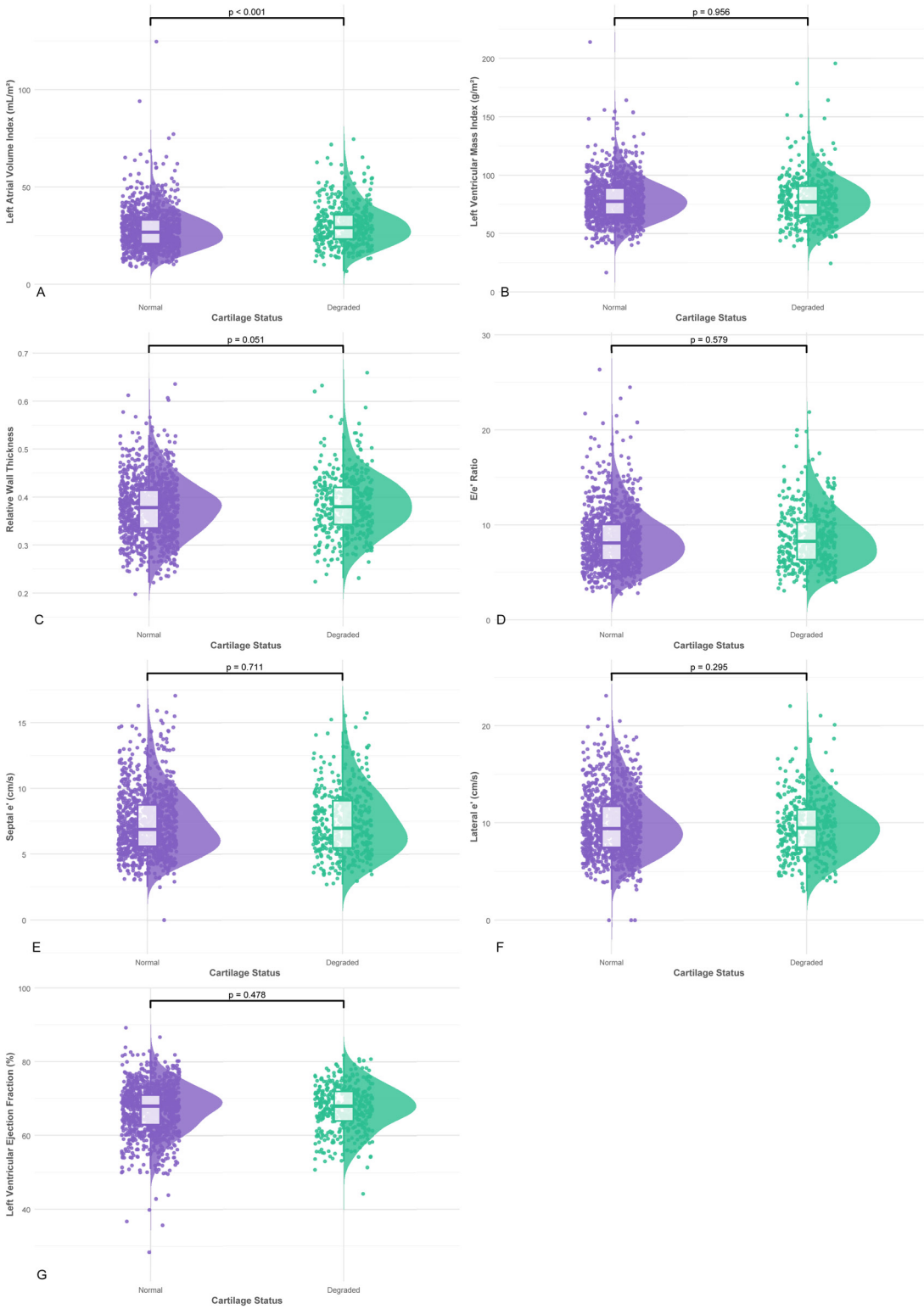

Figure 2. The comparison of cardiac parameters between normal and degraded cartilage groups by raincloud plots. Nonparametric Wilcoxon test was used to compare the differences between the 2 groups. (A) LAVI; (B) LVMI; (C) RWT; (D) mitral valve *E/e'* ratio; (E) septal *e'* velocity; (F) lateral *e'* velocity; (G) LVEF. LAVI = left atrial volume index; LVEF = left ventricular ejection fraction; LVMI = left ventricular mass index; RWT = relative wall thickness.

All data collected were anonymized and encrypted to protect the privacy of participants. Only authorized research staff had access to the data. The current study was reported according to the STROBE guideline for observational studies.

3. Results

3.1. Study population and baseline characteristics

The study included 1,471 participants (1,041 in the normal cartilage group and 430 in the degraded cartilage

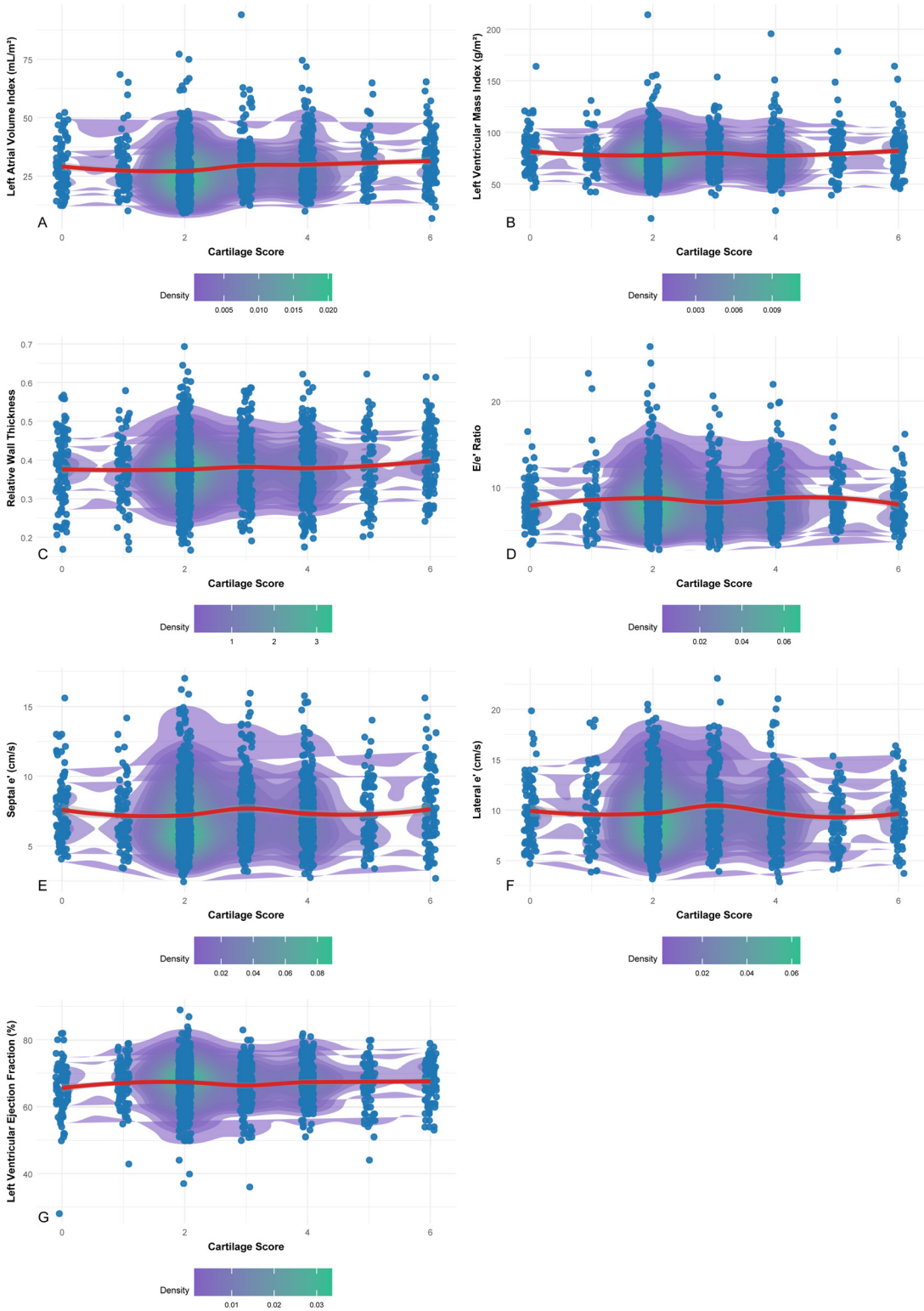

Figure 3. The distribution of cartilage degradation score and cardiac parameters. Plots use scatter points, 2D density polygons (color-coded for density), and loess fits (red line with 95% CI). (A) LAVI; (B) LVMI; (C). RWT; (D) mitral valve *E/e'* ratio; (E) septal *e'* velocity; (F) lateral *e'* velocity; (G) LVEF. CI = confidence interval; LVEF = left ventricular ejection fraction; LVMI = left ventricular mass index.

group) aged 35 to 75 years from the Longitudinal Investigation of Osteoarthritis and Cardiovascular Health Status cohort. The measurement of cartilage degradation and cardiac parameters were illustrated in Supplementary Figures 1, Supplemental Digital Content, https://links.lww.com/CARES/A1, and 2, Supplemental Digital Content, https://links.lww.com/CARES/A2, respectively. The distribution of cartilage degeneration score in the study population was displayed in Figure 1A. The bilateral kappa = 0.527,

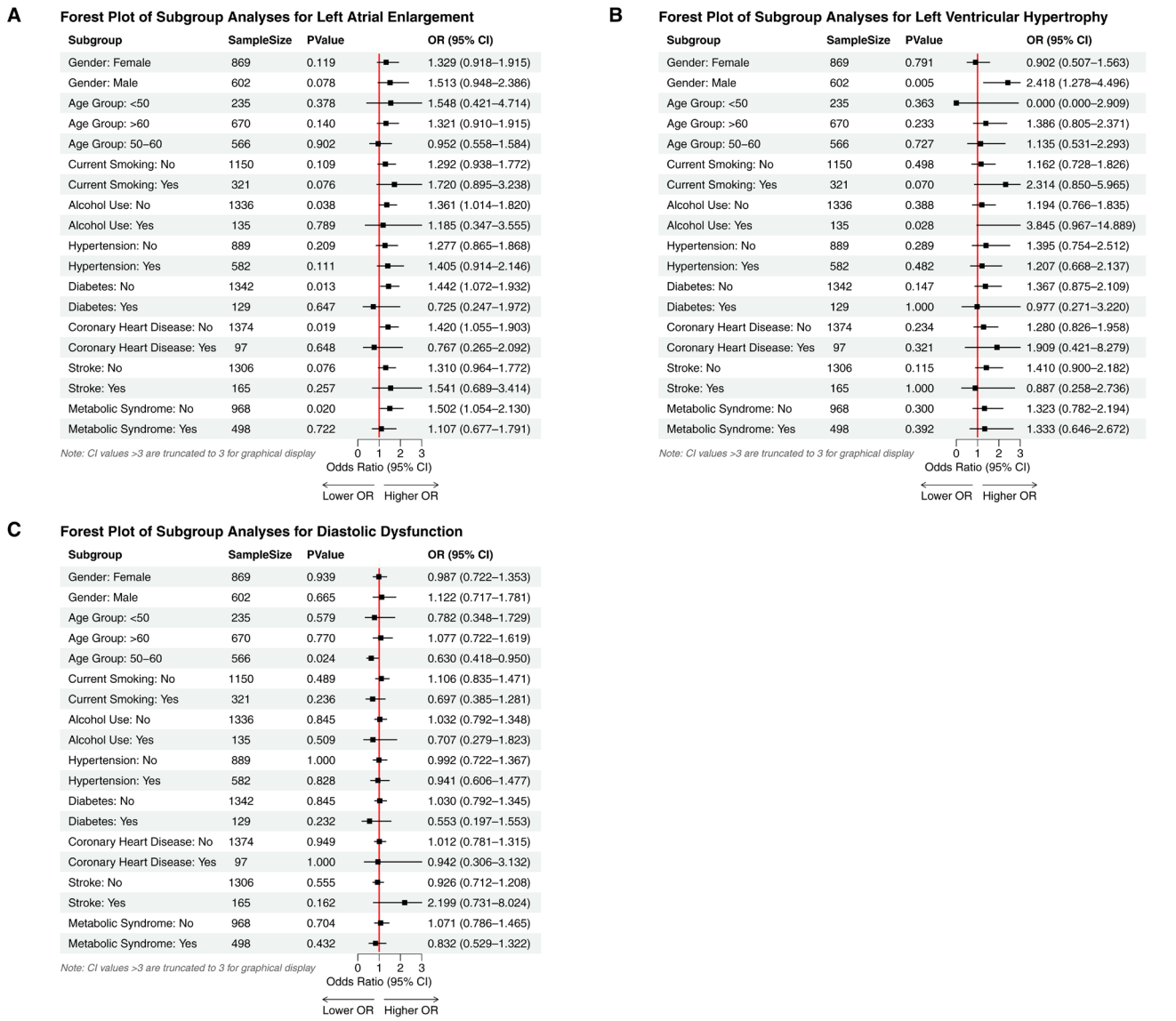

Figure 4. Forest plots to display the association between cartilage degradation and left atrial enlargement (A), left ventricular hypertrophy (B), and diastolic dysfunction (C).

indicating moderate symmetry. The cutoff value was 3.5, 4.5, and 3.5 for left atrial enlargement, left ventricular hypertrophy, and diastolic dysfunction, respectively (Fig. 1B–D). Taken together, we decided to use a cutoff value of ≥ 4 to define cartilage degradation. The degraded cartilage group (n = 430) was older (median age: 64 [interquartile range {IQR}: 56–69] vs. 58 [IQR: 52–67] years, $p < 0.001$) and had a lower male proportion (31% vs. 45%, $p < 0.001$). Significantly more participants in the degraded group were nonsmokers (84% vs. 76%, $p = 0.001$) and had diabetes (11% vs. 7.7%, $p = 0.029$). No differences were observed in lipid profiles, blood pressure, or body mass index between groups (Table 1). Cardiac structural differences were notable (Fig. 2): the degraded cartilage group exhibited higher LAVI (median: 29 [23–36] vs. 27 [21–33] mL/m², $p < 0.001$) and trend toward increased RWT (median: 0.38 [0.34–0.42] vs. 0.38 [0.34–0.41], $p = 0.051$). The median LVEF was 68% (IQR: 63%–71%) in the normal group and 68% (IQR: 64%–72%) in the degraded group ($p = 0.478$). LVMI medians were 78 g/m² (IQR: 67–89 g/m²) and 77 g/m² (IQR: 66–91 g/m²) ($p = 0.956$), while the mitral E/e' ratio was 8.10 (IQR: 6.32–10.06) vs. 8.27 (IQR: 6.35–10.31) ($p = 0.579$). Septal e' velocity medians were 6.91 cm/s (IQR: 5.61–8.77 cm/s) and 6.99 cm/s (IQR: 5.47–9.10 cm/s) ($p = 0.711$), and lateral e' velocity medians were 9.4 cm/s (IQR: 7.5–11.7 cm/s) vs. 9.5 cm/s (IQR: 7.5–11.4 cm/s) ($p = 0.295$). The distribution of cartilage degradation score and cardiac parameters were illustrated in Figure 3.

3.2. Subgroup and sensitivity analyses

In subgroup analyses (Fig. 4), cartilage degradation showed a consistent trend toward increased risk of left atrial enlargement in almost all subgroups except in

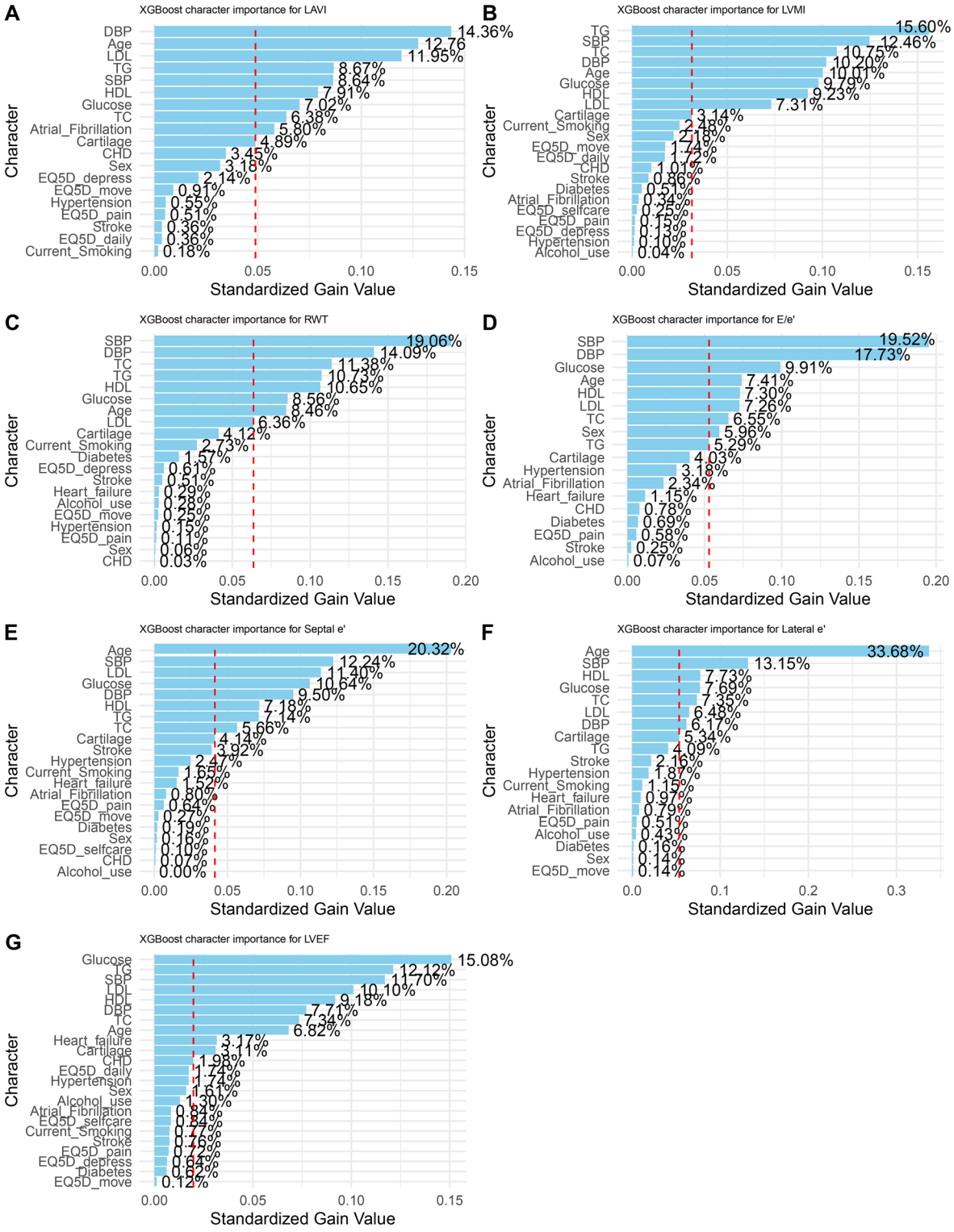

Figure 5. XGBoost based gain value to decide the importance of the cartilage degradation score in explaining the cardiac remodeling parameters. The accumulated gain value of over 90% was used as the cutoff value to choose the most important variables. (A) LAVI; (B) LVMI; (C) RWT; (D) mitral valve *E*/*e*' ratio; (E) septal *e*' velocity; (F) lateral *e*' velocity; (G) LVEF. LVEF = left ventricular ejection fraction; LVMI = left ventricular mass index.

those with a history of diabetes and CHD. Sensitivity analyses (Supplementary Table S1, Supplemental Digital Content, https://links.lww.com/CARES/A3) showed that cartilage degradation remained significantly associated with left atrial enlargement across all subgroups excluding participants with preexisting CHD (OR = 1.404, 95% CI = 1.054–1.862, $p = 0.019$), stroke (OR = 1.295, 95% CI = 0.964–1.732, $p = 0.083$), HF

(OR = 1.350, 95% CI = 1.026–1.768, $p = 0.030$), AF (OR = 1.397, 95% CI = 1.059–1.834, $p = 0.017$), or any CVD (OR = 1.449, 95% CI = 1.057–1.975, $p = 0.020$). By contrast, no significant associations were found for left ventricular hypertrophy or diastolic dysfunction across almost all subgroups and sensitivity analyses, reinforcing the specificity of cartilage degradation for atrial remodeling.

3.3. Machine learning analysis

XGBoost analysis identified cartilage degradation as an important contributor of LAVI, with a standardized gain value of 4.89 % (ranking 10th among 24 variables; Fig. 5A). For other parameters, cartilage degradation also exhibited substantial importance, with standardized gain values of 3.14% for LVMI (rank 9th), 6.36% for RWT (rank 8th), 5.29% for mitral *E*/*e*' ratio (rank 9th), 4.14% for septal *e*' velocity (rank 9th), 5.34% for lateral *e*' velocity (rank 8th), and 1.98% for LVEF (rank 11th). With the accumulated gain value of over 90% as the cutoff value to chose the most important variables, cartilage degradation was picked out for cardiac parameters including LAVI, LVMI, septal *e*' velocity, lateral *e*' velocity and LVEF.

4. Discussion

This cross-sectional study investigated the relationship between knee cartilage degeneration and cardiac structure and function in a cohort of middle-aged and elderly individuals. Although the cross-sectional design limits causal inferences, the findings offer valuable insights into this complex relationship.

4.1. Association between knee cartilage degeneration and left atrial enlargement

The significant positive association between knee cartilage degeneration and an increased LAVI is a crucial finding. An enlarged left atrium is a well-established risk factor for cardiovascular complications such as AF, HF, and stroke. In our study, participants with degraded knee cartilage had a higher median LAVI, these results, bolstered by machine learning analyses identifying cartilage degradation as a key contributor of LAVI, collectively suggest that cartilage health may serve as a novel biomarker for early atrial cardiac remodeling independent of traditional cardiovascular comorbidities. Moreover, knee pain and reduced mobility due to cartilage degeneration often led to decreased physical activity. This, in turn, is associated with an increased risk of CVDs and can contribute to left atrial enlargement through deconditioning, increased adiposity, and abnormal hemodynamics.[23] Additionally, shared risk factors such as obesity and MS, although adjusted to some extent, may still cause residual confounding, as obesity can accelerate cartilage degeneration and is a major risk factor for cardiovascular remodeling.[22–27]

4.2. Lack of association with other cardiac parameters

Our subgroup and sensitivity analyses consistently showed no significant association between cartilage degradation and left ventricular hypertrophy or diastolic dysfunction, across subgroups excluding participants with preexisting CVDs. This lack of association may be attributed to the early stage of cartilage degradation studied here may not yet induce detectable ventricular remodeling. Additionally, confounding factors such as age-related myocardial changes, hypertension, or diabetes-known to influence ventricular structure and diastolic function-could overshadow any subtle effects of cartilage degradation.

4.3. Strengths and limitations of the study

One strength of this study lies in the objective assessment of cartilage degeneration using ultrasound imaging, coupled with a detailed evaluation of cardiac structure and function strictly based on relevant guideline criteria. This approach enabled us to detect early subclinical manifestations, rather than relying solely on medical history and adverse events. By integrating objective imaging metrics with standardized cardiac assessments, the study enhances the accuracy of identifying preclinical abnormalities, which might otherwise remain undetected through conventional clinical evaluations. This dual methodology not only complements traditional assessment approaches but also provides a more comprehensive framework for understanding the early pathological continuum, thereby improving the sensitivity for capturing subtle changes in tissue and organ function before the onset of overt clinical symptoms or events.

Despite the valuable findings, this study has several limitations. First, the cross-sectional design of this study precludes definitive conclusions about causality, and reverse causality is plausible: Subclinical cardiac dysfunction might impair joint microcirculation or reduce physical activity, accelerating cartilage degradation, even in those without overt CVD. Residual confounding also persists. Unmeasured factors like inflammatory cytokines, objective physical activity data, visceral adiposity, genetic predispositions, or chronic stress could drive both phenotypes. Inflammation, physical inactivity, and metabolic dysfunction—proposed as shared pathways—do not exclude these alternatives. Our results reflect potential shared vulnerability, not direct causation. Besides, the observed associations at a single point are impossible to determine the direction of causality. Longitudinal studies tracking temporal sequences of cardiac and cartilage changes, with comprehensive measurement of intermediates, are needed to clarify directionality and address these uncertainties. This cohort is from 1 region in China, and OA/CVD prevalence or risk factors may differ elsewhere. Although we adjusted for multiple confounding factors, there may still be residual confounding. Unmeasured

factors such as inflammatory markers, genetic predisposition, diet, and psychological stress could influence both knee cartilage degeneration and cardiac parameters. The assessment of knee cartilage degeneration based on a specific scoring system of the intercondylar fossa cartilage may not fully represent the overall cartilage status of the knee joint. Different assessment methods may yield different results. Finally, the sample size, while relatively large, may still be insufficient to detect small but clinically significant associations, especially in subgroup analyses. Larger scale studies with more diverse populations are needed to confirm and generalize our findings.

4.4. Clinical implications and future directions

Our study highlights LAVI as a potential biomarker linking knee cartilage degeneration to cardiovascular risk, particularly in older adults and females. While potential biological mechanisms were not clear, it was suggested that the 2 diseases commonly co-occur in older adults, exceeding explanations by shared risk factors like age and obesity.[28] Mechanistically, OA-induced disability elevates CVD risk via reduced mobility, while low-grade inflammation underlies shared pathogenic pathways, particularly linking atherosclerosis to joint damage.[29,30] Synergistic effects exacerbate symptoms, highlighting intertwined molecular mechanisms and the need for integrated management.

Clinicians caring for OA patients should consider screening for atrial enlargement–an actionable target for preventing arrhythmias and HF-especially in those with advanced cartilage damage.

Future research should adopt longitudinal designs to clarify causality, incorporate multitissue joint imaging (osteophyte formation, meniscal extrusion, and others), and explore sex- and age-specific pathways (e.g., estrogen signaling, senescence). Additionally, randomized controlled trials evaluating whether OA treatments (e.g., exercise, anti-inflammatory therapies) mitigate cardiac remodeling could inform integrated management strategies for this high-risk population.

This study provides evidence that knee cartilage degeneration is associated with cardiac remodeling parameters, which serve as crucial indicators of cardiovascular risk. These results suggest that structural joint damage in OA may be linked to subclinical cardiac remodeling, thereby highlighting the importance of further research to explore this association in depth. While these findings underscore the need to consider OA as a systemic disease, definitive recommendations for proactive cardiovascular screening in patients with structural joint damage are premature. Instead, this study emphasizes the necessity for future research to investigate the potential integration of cardiovascular risk assessment into the management of OA, offering a foundation for future exploration of comprehensive care strategies.

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During the preparation of this work, the authors used Doubao, an AI language model, in order to assist with English language polishing. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Ethical statement

The study protocol was approved by the institutional review board (IRB) of Luohe Central Hospital on April 13, 2023 (approval number 2023010). All participants provided written informed consent. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

Haoran Wang: Contributed to study conception, data analysis, manuscript drafting and revision, and provided statistical expertise. Qichao Wang: Participated in study design, data analysis, manuscript writing and revision from an orthopedic view. Bing He and Jing Bai: Collected and assembled data. Nan Wang, Jin Wang and Dongliang Liu: Gathered and organized data, and provided logistical and administrative help. Qiaotao Xie: Contributed to study design, manuscript review, and funding acquisition. Haoran Wang and Qiaotao Xie are responsible for the work's integrity.

References

[1] Allen KD, Thoma LM, Golightly YM. Epidemiology of osteoarthritis. Osteoarthr Cartil. 2022;30:184–95.

[2] Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee

osteoarthritis in population-based studies. EClinicalMedicine. 2020;29-30:100587.
[3] Goldring MB, Otero M. Inflammation in osteoarthritis. Curr Opin Rheumatol. 2011;23:471–8.
[4] Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet (London, England). 2019;393:1745–59.
[5] Tsao CW, Aday AW, Almarzooq ZI, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2023 update: a report from the American Heart Association. Circulation. 2023;147:e93–e621.
[6] Fernandes GS, Valdes AM. Cardiovascular disease and osteoarthritis: common pathways and patient outcomes. Eur J Clin Invest. 2015;45:405–14.
[7] Benito MJ, Veale DJ, FitzGerald O, van den Berg WB, Bresnihan B. Synovial tissue inflammation in early and late osteoarthritis. Ann Rheum Dis. 2005;64:1263–7.
[8] Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. Nature. 2011;473:317–25.
[9] Wang H, Bai J, He B, Hu X, Liu D. Osteoarthritis and the risk of cardiovascular disease: a meta-analysis of observational studies. Sci Rep. 2016;6:39672.
[10] Barbour KE, Lui LY, Nevitt MC, et al.; Study of Osteoporotic Fractures Research Group. Hip osteoarthritis and the risk of all-cause and disease-specific mortality in older women: a population-based cohort study. Arthritis Rheumatol. 2015;67:1798–805.
[11] Haugen IK, Ramachandran VS, Misra D, et al. Hand osteoarthritis in relation to mortality and incidence of cardiovascular disease: data from the Framingham heart study. Ann Rheum Dis. 2015;74:74–81.
[12] Hoeven TA, Leening MJG, Bindels PJ, et al. Disability and not osteoarthritis predicts cardiovascular disease: a prospective population-based cohort study. Ann Rheum Dis. 2015;74:752–6.
[13] Jonsson H, Helgadottir GP, Aspelund T, et al. Hand osteoarthritis in older women is associated with carotid and coronary atherosclerosis: the AGES Reykjavik study. Ann Rheum Dis. 2009;68:1696–700.
[14] Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. BMJ. 2011;342:d1165.
[15] Rahman MM, Kopec JA, Cibere J, Goldsmith CH, Anis AH. The relationship between osteoarthritis and cardiovascular disease in a population health survey: a cross-sectional study. BMJ Open. 2013;3:e002624.
[16] Lisee C, McGrath ML, Kuenze C, et al. Reliability of a novel semiautomated ultrasound segmentation technique for assessing average regional femoral articular cartilage thickness. J Sport Rehabil. 2020;29:1042–6.
[17] Lye TH, Gachouch O, Renner L, et al. Quantitative ultrasound assessment of early osteoarthritis in human articular cartilage using a high-frequency linear array transducer. Ultrasound Med Biol. 2022;48:1429–40.
[18] Oo WM, Bo MT. Role of ultrasonography in knee osteoarthritis. J Clin Rheumatol. 2016;22:324–9.
[19] Saarakkala S, Waris P, Waris V, et al. Diagnostic performance of knee ultrasonography for detecting degenerative changes of articular cartilage. Osteoarthr Cartil. 2012;20:376–81.
[20] Chinese Society of Cardiology Chinese Medical Association Chinese College of Cardiovascular Physician Chinese Heart Failure Association of Chinese Medical Doctor Association, Editorial Board of Chinese Journal of Cardiology. [Chinese guidelines for the diagnosis and treatment of heart failure 2024]. Zhonghua Xin Xue Guan Bing Za Zhi. 2024;52:235–75.
[21] Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1–39.e14.
[22] Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr. 2009;22:107–33.
[23] Heitmann KA, Løchen ML, Stylidis M, Hopstock LA, Schirmer H, Morseth B. Associations between physical activity, left atrial size and incident atrial fibrillation: the Tromsø Study 1994-2016. Open Heart. 2022;9:e001823.
[24] Abel ED, Litwin SE, Sweeney G. Cardiac remodeling in obesity. Physiol Rev. 2008;88:389–419.
[25] Aurigemma GP, de Simone G, Fitzgibbons TP. Cardiac remodeling in obesity. Circ Cardiovasc Imaging. 2013;6:142–52.
[26] Preda A, Liberale L, Montecucco F. Imaging techniques for the assessment of adverse cardiac remodeling in metabolic syndrome. Heart Fail Rev. 2022;27:1883–97.
[27] Fitchett D, Connelly KA. Impaired cardiac function in metabolic syndrome. Can J Cardiol. 2014;30:270–1.
[28] Fernandes GS, Valdes AM. Cardiovascular disease and osteoarthritis: common pathways and patient outcomes. Eur J Clin Invest. 2015;45:405–14.
[29] Sampath SJP, Venkatesan V, Ghosh S, Kotikalapudi N. Obesity, metabolic syndrome, and osteoarthritis-an updated review. Curr Obes Rep. 2023;12:308–31.
[30] Motta F, Barone E, Sica A, Selmi C. Inflammaging and Osteoarthritis. Clin Rev Allergy Immunol. 2023;64:222–38.