Journal of the American Heart Association

ORIGINAL RESEARCH

Periodontal Disease Associated With Interstitial Myocardial Fibrosis: The Multiethnic Study of Atherosclerosis

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BACKGROUND: Periodontitis is a chronic inflammatory disease common among adults. It has been suggested that periodontal disease (PD) may be a contributing risk factor for cardiovascular disease; however, pathways underlying such a relationship require further investigation.

METHODS AND RESULTS: A total of 665 men (mean age 68±9 years) and 611 women (mean age 67±9 years) enrolled in the MESA (Multiethnic Study of Atherosclerosis) underwent PD assessment using a 2-item questionnaire at baseline (2000–2002) and had cardiovascular magnetic resonance 10 years later. PD was defined when participants reported either a history of periodontitis or gum disease or lost teeth caused by periodontitis or gum disease. Multivariable linear regression models were constructed to assess the associations of baseline self-reported PD with cardiovascular magnetic resonance–obtained measures of interstitial myocardial fibrosis (IMF), including extracellular volume and native T1 time. Men with a self-reported history of PD had greater extracellular volume percent (ß=0.6%±0.2, *P*=0.01). This association was independent of age, left ventricular mass, traditional cardiovascular risk factors, and history of myocardial infarction. In a subsequent model, substituting myocardial infarction for coronary artery calcium score, the association of PD with IMF remained significant (ß=0.6%±0.3, *P*=0.03). In women, a self-reported history of PD was not linked to higher IMF. Importantly, a self-reported history of PD was not found to be associated with myocardial scar independent of sex (odds ratio, 1.01 [95% CI, 0.62–1.65]; *P*=0.9).

CONCLUSIONS: In a community-based setting, men but not women with a self-reported PD history at baseline were found to be associated with increased measures of IMF. These findings support a plausible link between PD, a proinflammatory condition, and subclinical IMF.

Key Words: magnetic resonance imaging ■ myocardial fibrosis ■ periodontal disease ■ sex

Interstitial myocardial fibrosis (IMF) is considered a typical feature of cardiac remodeling and a prognostic marker for cardiovascular dysfunction.[1,2] Cardiac remodeling involves abnormal extracellular matrix network changes and hypertrophic changes in cardiac myocytes.[3] Subclinical myocardial fibrosis significantly contributes to the development of heart failure and end-stage cardiovascular disease (CVD).[4] Risk factors for diffuse interstitial fibrosis include modifiable and nonmodifiable cardiovascular risk factors.[5]

Periodontal disease (PD), the sixth most common human disease, affects 20% to 50% of the world's population and 42% of US adults >30 years of age.[6–8] It is defined as a chronic inflammatory condition caused by bacterial infection, affecting the surrounding structure of the teeth (gingival tissue, periodontal ligament,

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Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.122.027974

For Sources of Funding and Disclosures, see page 7.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- In a community-based multiethnic population, a history of periodontal disease in men reported at the initial visit was independently associated with increased measures of interstitial myocardial fibrosis by cardiac magnetic resonance imaging T1 mapping 10 years later.

What Are the Clinical Implications?

- Interstitial myocardial fibrosis is a hallmark of cardiac remodeling and predicts poor outcomes.
- Periodontal disease could be a potential gateway for interstitial cardiac fibrosis, which in turn is a known substrate for cardiovascular disease including heart failure with preserved ejection fraction.
- The article suggests the need for a better focus on oral health and its role in subclinical cardiovascular diseases and heart disease prevention.

Nonstandard Abbreviations and Acronyms

ECV	extracellular volume
IMF	interstitial myocardial fibrosis
MESA	Multiethnic Study of Atherosclerosis
PD	periodontal disease

and bone), possibly leading to tooth loss and potential systemic inflammation.[9,10]

It has been suggested that PD may be a contributing risk factor for CVD.[11] Although many studies have found associations between periodontitis and CVD, the relationship is still debated and requires more investigation.[12,13] Moreover, to our knowledge, no studies have established associations between PD and myocardial fibrosis, except experimental studies in mice.[3,14,15]

Therefore, we aimed to use the MESA (Multiethnic Study of Atherosclerosis) population to assess the relationship between self-reported PD at Visit 1 and IMF at Exam 5, 10 years later.

METHODS

Data Availability

The data underlying this article were obtained as part of the National Institutes of Health– sponsored MESA by permission. Data will be shared on request to the corresponding author with permission of the MESA steering committee.

Anonymized data and materials have been made publicly available at BioLincc and can be accessed at https://biolincc.nhlbi.nih.gov/home/.

Study Design and Population

The MESA is a multicenter, community-based, prospective study that enrolled 6814 men and women from different racial and ethnic groups (non-Hispanic White, Black, Hispanic, and Asian). At baseline (July 2000 to August 2002), participants were recruited from different study sites in the United States (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan, NY; and St. Paul, MN). Their ages ranged from 45 to 84 years, and they were free from CVD. The MESA design, objectives, and methods have been described comprehensively.[16] A 10-year follow-up was performed on this cohort over 5 examinations. In the fifth visit 10 years later (MESA 5, 2010–2012), 4716 out of the 6814 participants completed the visit. Among the latter, 3015 received cardiac magnetic imaging (MRI). Of those, 1345 underwent late gadolinium enhancement assessment and T1 mapping using the modified Look-Locker inversion recovery sequence at 5 clinical sites (Johns Hopkins University, Baltimore, MD; University of Minnesota, Minneapolis, MN; Northwestern University, Chicago, IL; Wake Forest University, Winston-Salem, NC; and University of California, Los Angeles, CA). Participants who had available data on PD assessed at baseline were included in the analysis. Subjects with missing follow-up data or missing information on any of the covariates incorporated in the multivariable regression models were excluded (N=1276). The institutional review boards approved the study at each site, and all participants gave informed consent.

Exposure of Interest

PD, the exposure of interest, was assessed at Visit 1 using a self-reported questionnaire. Self-reported PD has been shown to have acceptable validity.[17] Participants had to answer 2 questions: (1) whether they had a history of periodontitis or gum disease and (2) whether they had lost teeth caused by periodontitis or gum disease.[13,18,19] If they had an affirmative response to 1 of the 2 questions, they were classified as having PD. Patients with missing information or who responded that they did not know to any of the questions were excluded from the study.

Outcome of Interest

Interstitial Myocardial Fibrosis

IMF was assessed at Visit 5 using the single breath-hold modified Look-Locker inversion recovery

sequence. The MRI protocol has been previously described in other studies.[20,21] All images were evaluated in a blinded process at the MRI laboratory at Johns Hopkins University, Baltimore, Maryland. Using the MASS research software (Department of Radiology, Leiden University Medical Center, Leiden, the Netherlands), and T1 maps were constructed offline. T1 times were calculated using the Levenberg-Marquardt algorithm, in which a 3-parameter curve of the modified Look-Locker inversion images was fitted. These included native T1 (precontrast) and T1 at 12 and 25 minutes (postcontrast). The partition coefficient was calculated by plotting 1/T1 myocardium versus 1/T1 blood of the 3 predetermined time points. After that, the partition coefficient was multiplied by 1-hematocrit to generate the synthetic extracellular volume (ECV) fraction.[22] A thorough description of native T1 and synthetic ECV measures was explained and used in previous MESA studies.[20,21] To define IMF, we used native T1 time and ECV percentage as a reference.[23] Greater ECV percentage and native T1 time highlight diffuse myocardial fibrosis.[24]

Myocardial Scar

Using late gadolinium enhancement after 15 minutes of contrast administration (0.15 mmol of intravenous gadopentetate dimeglumine [Magnevist; Bayer Healthcare Pharmaceuticals, Montville, NJ]), a myocardial scar was defined through a focal enhancement in 2 adjacent short-axis slices or 1 short-axis and a long-axis image at the exact location.[25] Manually, using the QMass research software (version 7.2; Medis, Leiden, the Netherlands), myocardial scars were quantified as a percentage of left ventricular mass. Typical scars were considered ischemic in nature if they involved the subendocardium in coronary artery distribution. In contrast, if they involved the subepicardium or midwall, they would be atypical or nonischemic. Using the full width at half-maximum criterion, the area of the myocardial scar was manually defined as the area with increased signal intensity.[26,27] Our cohort had a total of 111 (9%) myocardial scars. Studies that evaluated myocardial scar in the MESA have been previously published.[25,26,28]

Statistical Analysis

There was a significant effect modification by sex ($P<0.05$) on the association between PD and markers of IMF; therefore, all assessments were stratified by sex. Categorical variables were described as frequency or percentages and compared using the Pearson χ^2 test. Continuous variables were presented as mean±standard deviation or median with the interquartile range depending on the normality of the data and compared using a *t* test. Multivariable linear models were constructed by adding the variables in a stepwise increasing degree of adjustment to study the associations and mechanisim between PD and cardiovascular magnetic resonance (CMR) measures of IMF (ECV and native T1). Covariates included in the model were selected based on the time of the evaluation for myocardial fibrosis at Exam 5, and the self-reported exposure history of PD was retained in all models. In addition, a sensitivity analysis was performed by analyzing the association of CMR measures of IMF (ECV and native T1) at Exam 5 with covariates that were evaluated at Exam 1 at baseline (Tables S1 and S2). Similarly, multivariable logistic regression was implemented to study the association between PD and myocardial scar using the same covariates used in the models with IMF. A 2-sided $P<0.05$ was considered statistically significant. All analyses were done using Stata 17 (Stata Statistical Software, release 17; StataCorp, College Station, TX), and figures were created with BioRender.com.

RESULTS

In this study, the MESA subpopulation consisted of 1276 participants divided into 665 (52.1%) men and 611 (47.9%) women. They all had complete PD assessment and follow-up measures of myocardial T1 time performed 10 years later. The baseline characteristics of the study population stratified by sex are highlighted in Table 1. Men had a mean age of 68±9 years and racial and ethnic distribution of 51% White, 23% Black, 15% Hispanic, and 11% Chinese American. As for women, their mean age was 67±9 years, and they had a similar racial distribution as men, with the most frequent race and ethnicity being White (54%), followed by Black (23%), then Hispanic (12%), and finally Chinese American (10%). Compared with women, men had unfavorable smoking profiles (33% of men were nonsmokers compared with 53% of women; 58% of men were former smokers, with 40% for women; 9% of men were current smokers, with 7% for women; $P<0.001$). However, the prevalence of men without diabetes was lower compared with women (58% versus 70%; $P<0.001$), but a higher percentage of men were being treated for diabetes (15% versus 13%; $P<0.001$). Both sexes shared the same percentage of impaired fasting glucose (26%) and being without treatment for diabetes (1%). Also, men had higher diastolic blood pressure (71 mm Hg versus 65 mm Hg in women; $P<0.001$), lower high-density lipoprotein levels (49 mg/dL versus 60 mg/dL in women; $P<0.001$), and lower low-density lipoprotein levels compared with women (100 mg/dL versus 111 mg/dL in women; $P<0.001$).

Cardiac MRI measures also differed by sex. Men had greater left ventricular end-systolic and diastolic volumes, left ventricular mass, and myocardial scar prevalence than women. However, they showed lower left ventricular ejection fraction, and on T1 mapping had less extracellular

Table 1. Baseline Characteristics Stratified by Sex

Characteristic	Men, n=665	Women, n=611	*P* value
Age, y	68±9	67±9	0.2
Body mass index, kg/m^2	28.2±4.5	28.5±6	0.3
Periodontal disease*	192 (29)	164 (27)	0.4
Race and ethnicity (%)			
White	342 (51)	332 (54)	0.5
Black	150 (23)	141 (23)	
Chinese American	72 (11)	62 (10)	
Hispanic	101 (15)	76 (12)	
Tobacco use (%)			
Never	220 (33)	321 (53)	<0.001
Former	384 (58)	247 (40)	
Current	61 (9)	43 (7)	
Diabetes status (%)			
None	385 (58)	426 (70)	<0.001
Impaired fasting glucose	171 (26)	96 (26)	
Untreated diabetes	7 (1)	7 (1)	
Treated diabetes	102 (15)	82 (13)	
Heart rate, bpm	65±10	64±11	0.07
Systolic blood pressure, mm Hg	121±18	122±20	0.5
Diastolic blood pressure, mm Hg	71±9	65±9	<0.001
Hypertension medication, n (%)	328 (49)	305 (50)	0.8
LDL cholesterol, mg/dL	100±30	111±31	<0.001
HDL cholesterol, mg/dL	49±13	60±17	<0.001
Lipid-lowering medication, n (%)	275 (41)	225 (37)	0.1
eGFR, mL/min per 1.73 m^2	84±17	85±20	0.2
MRI cardiac measures‡			
LV end-systolic volume index, mL/m^2†	28±10	22±6	<0.001
LV end-diastolic volume index, mL/m^2†	69±15	62±11	<0.001
LV mass index, g/m^2*,†	73±12	58±9	<0.001
LV ejection fraction, %	59.5±7.2	64.1±6.1	<0.001
ECV, %	26.2±2.7	27.4±2.9	<0.001
Native T1, ms	969±38	989±45	<0.001
Myocardial scar, %	96 (14.5)	15 (2.45)	<0.001
CAC, Agatston units	108 (5–492)	12 (0–101)	<0.001

CAC indicates coronary artery calcium; ECV, extracellular volume; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LV, left ventricular; and MRI, magnetic resonance imaging.

*P value <0.001 comparing characteristics of men and women.

†LV volumes and mass are indexed to body surface area.

‡Measured at exam visit 5 (2010–2012).

volume (ECV%) and native T1 than women (P<0.001) (Table 1). Moreover, among men, a significant association was found between baseline assessment of PD and CMR measures of IMF (ECV %) (Table 2). In a fully adjusted model (Model 3), men with a self-reported history of PD had higher ECV (P=0.01) after controlling for baseline characteristics, cardiovascular risk factors, interim cardiovascular events, and socioeconomic status. Importantly, in additional fully adjusted models (Model 4), substituting interim cardiovascular events (such as myocardial infarction) for coronary artery calcium score, the association between PD and ECV remained significant (β=0.6±0.3, P=0.03) (Table 2). Similar associations were observed when CMR measures of diffuse myocardial fibrosis after adjustment for covariates from baseline visit evaluation (Tables S1 and S2) were evaluated. In contrast, there was no association between baseline assessment of PD and ECV or native T1 values among women (Table 3). Finally, there was no association between baseline assessment of PD and myocardial scar independent of sex (odds ratio, 1.01 [95% CI, 0.62–1.65]; P=0.9) (Table 4).

DISCUSSION

To our knowledge, this study is the first multiethnic, multicenter population-based study to describe the association between PD and IMF estimated by T1 mapping. Self-reported PD was associated with greater IMF measures (ECV %) in men but not in women. These findings might underscore PD's structural impact on the myocardium as a focus of persistent inflammation. IMF, measured by T1 mapping, is a new and sensitive indicator of early tissue alterations in myocardial disease and other inflammatory disorders (Table S3). It also carries prognostic value for cardiovascular outcomes.[23,24] Recognizing PD as a morbid condition associated with IMF in a healthy population devoid of CVD may aid in underlining the different mechanisms related to the pathogenesis of cardiovascular disease, notably heart failure, potentially allowing improved prevention and intervention.

Many gram-negative anaerobic bacteria are involved in PD, such as *Porphyromonas gingivalis*, *Tannerella forsythensis*, *Actinobacillus actinomycetemcomitans*, *Campylobacter rectus*, *Prevotella intermedia*, and *Fusobacterium nucleatum*, and are found in the oral cavity within a complex biofilm known as dental plaque. A myriad of factors facilitates the translocation of bacteria to the oral cavity, leading to transient bacteremia and bacterial invasion of endothelial cells. Triggering mechanisms can be mechanical, such as brushing and mastication, or related to the highly vascularized and dilated nature of the periodontal vasculature initiated by the inflammatory condition created by PD.[29,30] Importantly, similar bacterial burden, such as those microorganisms found in PD, has

Table 2. Multivariable Association Between Baseline Assessment of Periodontal Disease and T1-Mapping Measures (Native T1 Mapping and ECV Fraction) in Men

Men				
Regression models	ECV, %		Native T1, ms	
	ß±SE	*P* value	ß±SE	*P* value
Model 1	0.6±0.2	0.01	3.5±3.3	0.4
Model 2	0.6±0.2	0.015	2.5±3.2	0.3
Model 3	0.6±0.2	0.01	3.0±3.2	0.3
Model 4	0.6±0.3	0.03	1.6±3.7	0.9

Model 1: Unadjusted.
Model 2: Adjusted for age, race, body mass index.
Model 3: Adjusted for variables included in Model 2, lipid-lowering therapy, low-density lipoprotein, systolic and diastolic blood pressure, any hypertensive medication, diabetes status, education, income, smoking status, estimated glomerular filtration rate;, history of myocardial infarction.
Model 4: Adjusted for variables included in Model 3, except the substituted history of myocardial infarction with total Agatston calcium score.
Covariates were selected at the time of the magnetic resonance imaging examination in MESA 5, except for periodontal disease, which was available only at the baseline initial visit. ECV indicates extracellular volume.

been reported in association with subclinical atherosclerosis, independent of traditional cardiovascular risk factors.[31] Furthermore, the periodontal pathogen *Porphyromonas gingivalis* has been shown to accelerate the development of myocardial remodeling and promote cardiac fibrosis in mice.[3,14]

Link Between Periodontal Inflammation, IMF, and CVD

The anaerobic bacteria biofilm in the periodontal pockets initiates an inflammatory cascade that releases proinflammatory cytokines, such as interferon-γ, interleukin (IL)-17, tumor necrosis factor, IL-1, and IL-6. At first, this inflammatory response aims at protecting the individual against bacterial invasion.[32] However, when the inflammation becomes chronic and uncontrolled, it leads to the irreversible destruction of the periodontal supporting tissues and the loss of alveolar bone.[33] Consequently, an intensified immune cell response penetrates the connective tissue adjacent to the periodontal pockets, acting as a reservoir of bacteria and their products.[34] When inflammatory mediators enter the systemic circulation, they affect distant organs, disturb the inflammatory equilibrium state, and enhance oxidative stress processes, leading to increased values of C-reactive protein, and other inflammatory markers in patients with periodontitis.[34,35] Several studies have demonstrated the association between PD and CVD across different populations.[36] Individuals with periodontitis tend to have an elevated risk of developing coronary artery disease, stroke, myocardial infarction, and atherosclerosis, even after adjusting for cardiovascular risk factors.[37] Also, individuals with periodontitis have been found to have a higher risk of atrial fibrillation and heart failure.[38,39] PD and CVD are multifactorial and have in common multiple risk factors such as age, smoking, socioeconomic status, diabetes, obesity, hypertension, stress, and many others, with inflammation playing a primordial role in their pathogenesis (Figure).[40] Patients with periodontitis exhibit higher inflammatory biomarkers, mainly C-reactive protein, tumor necrosis factor, and IL-6. Interestingly, the latter has been shown to play a central role in the fibrogenic pathway of the heart and has been independently linked to an increased CVD risk.[41–43] Moreover, IL-6 and C-reactive protein levels have been associated with myocardial fibrosis in men.[21] In our study, self-reported PD was positively related to IMF, measured by ECV among men. This finding highlights the impact of PD in causing pathological

Table 3. Multivariable Association Between Baseline Assessment of Periodontal Disease and T1-Mapping Measures (Native T1 Mapping and ECV Fraction) in Women

Women				
Regression models	ECV, %		Native T1, ms	
	ß±SE	*P* value	ß±SE	*P* value
Model 1	−0.1±0.2	0.5	6.5±4.1	0.1
Model 2	−0.1±0.2	0.5	6.3±4.1	0.1
Model 3	−0.2±0.25	0.3	3.8±4.2	0.4
Model 4	−0.1±0.3	0.6	7.0±4.8	0.1

Model 1: Unadjusted.
Model 2: Adjusted for age, race, body mass index.
Model 3: Adjusted for variables included in Model 2, lipid-lowering therapy, low-density lipoprotein, systolic and diastolic blood pressure, any hypertensive medication, diabetes status, education, income, smoking status, estimated glomerular filtration rate, history of myocardial infarction.
Model 4: Adjusted for variables included in Model 3, except the substituted history of myocardial infarction with total Agatston calcium score.
Covariates were selected at the time of the magnetic resonance imaging examination in MESA 5, except for periodontal disease, which was available only at the baseline initial visit. ECV indicates extracellular volume.

Table 4. Relationship Between Periodontal Disease at Exam 1 and the Presence of Myocardial Scar Measured for Those Who Had Available Late Gadolinium Enhancement Analysis

Myocardial scar		
	Periodontal disease	
	Odds ratio (95% CI)	*P* value
Model 1	1.10 (0.71–1.69)	0.6
Model 2	1.11 (0.71–1.73)	0.6
Model 3	1.01 (0.62–1.65)	0.9

Model 1: Unadjusted.
Model 2: Adjusted for age, race, body mass index.
Model 3: Adjusted for variables included in Model 2, lipid-lowering therapy, low-density lipoprotein, systolic and diastolic blood pressure, any hypertensive medication, diabetes status, education, income, smoking status, estimated glomerular filtration rate, history of myocardial infarction.

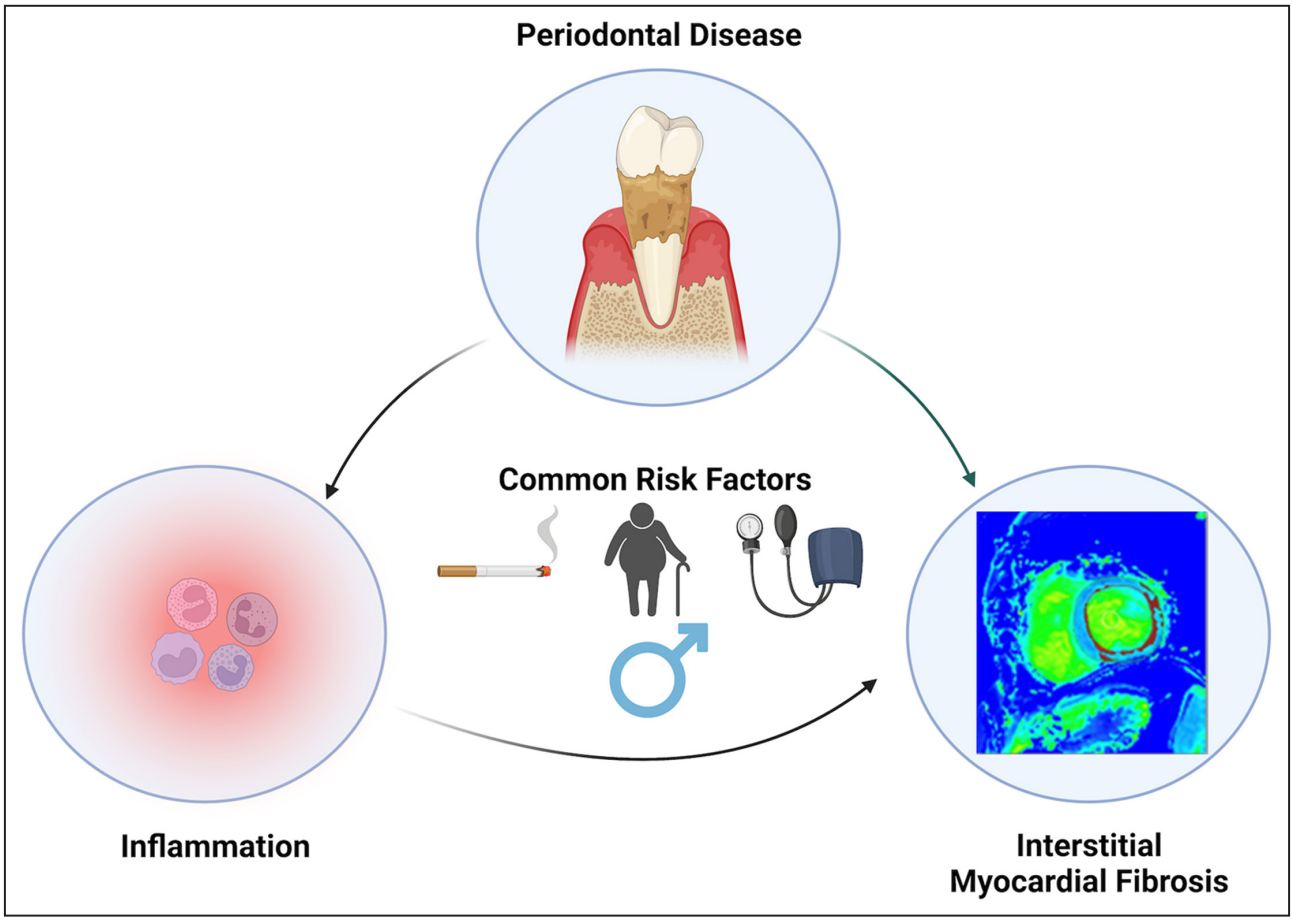

Figure. Study summary.
Traditional cardiovascular risk factors along with aging are associated with higher interstitial myocardial fibrosis through increased systemic inflammation. In the MESA (Multiethnic Study of Atherosclerosis) population, men with self-reported history of periodontal disease were found to have greater ECV percentages. The link between periodontal disease and interstitial myocardial fibrosis could be mediated through increased systemic inflammation.

changes in the myocardial extracellular matrix that characterize IMF through its underlying inflammatory component.[44] However, in our study, PD was not associated with myocardial scar or replacement fibrosis. IMF usually has a progressive onset and follows an increase in collagen synthesis by myofibroblasts under the influence of various stimuli (eg, aging, smoking, diabetes), and in our study we found that PD could be an additional stimulus that could play a role in expanding the extracellular matrix that precedes the later stage of end-stage myocardial replacement fibrosis.[45]

Sex, PD, and IMF

Although both men and women had similar percentages of PD at baseline (29% and 27%, respectively), PD was associated with IMF exclusively in men. Epidemiological data have shown that PD and progressive IMF display sexual dimorphism, wherein men are at greater risk for developing both diseases than women.[46–48] Many explanations have been proposed to clarify sex and oral health disparities. First, men seek preventive care less often than women.[49] The latter, display more positive attitudes and behaviors toward dental care, have greater oral health literacy, and are 26% more likely to floss regularly compared with men.[50,51] Second, men tend to use tobacco products at a higher rate than women,[52] and smoking has been found to have detrimental effects on the incidence and progression of PD.[53] However, epidemiologic studies have shown that men are at a heightened risk of periodontitis even after adjusting for behavioral and environmental factors.[54] Hence, sexual dimorphism in susceptibility to PD might be further explained by differential gene regulation, specifically steroid-responsive sex genes, operating through underlying inflammatory and immune responses.[55] Many genes on the X chromosome (including genes for cytokine receptors and immune-related proteins) might explain sex differences in immunity.[56] In regard to

inflammatory cytokine production, the innate immune response to pathogens appears to be increased in men compared with women, paralleling sex-specific differences in periodontitis.[55] Moreover, sex hormones have been shown to exhibit different effects on immunological components controlling not only the intensification but also the abatement of inflammation.[55] When facing antigens, humoral immunity in women seems to be more effective in terms of higher B-lymphocytic activation and antibody production compared with men, providing a protective component to women against inflammation and potentially PD and its ramifications.[57] Interestingly, the sexual difference in immune function, whether innate or adaptive, manifests in the aging process, supporting women in terms of longevity across species.[58] Moreover, recent experimental and epidemiological studies have found that there is a significant sex difference in markers of IMF, with most data highlighting men as having a more extracellular matrix– and fibrosis-related gene induction than women when exposed to increased inflammatory states.[20,21,47,48]

LIMITATIONS

Limitations influencing our analysis include the fact that PD was only measured at baseline; hence, we were not able to account for possible changes in periodontal severity and status during follow-up. Furthermore, PD was self-reported by participants themselves via a short questionnaire. Although self-reported PD has been validated in epidemiological studies, assessment by dental health professionals remains the gold standard for diagnosing PD.[17,59] Furthermore, notwithstanding thorough adjustments for possible confounding risk factors, we cannot exclude the possibility of potential unmeasured confounders such as access to dental insurance; however, we did control for several determinants of socioeconomic status such as income and education. Moreover, given the cross-sectional study design, temporal and selection bias between the initial examination and follow-up visits might have occurred. Thus, a healthier group of participants might have received a CMR contrast agent compared with others who were not eligible or declined. Finally, myocardial fibrosis was measured via native T1 and ECV, which are not for specific pathological processes.[23] Frequently, extracellular matrix expansion results from increased fibrosis, which may be attributable to diverse conditions such as hypertrophy, edema, or other types of cardiac pathologies.[24] In addition, data related to recent viral-induced myocarditis or myocardial infarction within 3 to 6 months of the scan were not available. Nevertheless, these MRI measurements offer consistent and conservative alternatives to assess myocardial fibrosis.[21] Finally, given this cross-sectional study, we cannot draw a causal link between PD and IMF.

CONCLUSIONS

In a community-based setting, using CMR measurements of IMF, men with a self-reported PD history at baseline were found to have greater ECV after 10 years of follow-up. This association was independent of age, traditional CVD risk factors, interim cardiovascular events, coronary artery calcium score, and socioeconomic status. These findings support the plausible link between PD, a proinflammatory condition, and subclinical IMF.

ARTICLE INFORMATION

Received August 27, 2022; accepted December 12, 2022.

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Acknowledgments

The authors thank the other investigators, the staff, and the participants of the MESA for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org. The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute, the National Institutes of Health, or the US Department of Health and Human Services.

Sources of Funding

This research was supported by contracts N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC95167, N01-HC-95168, and N01-HC-95169 from the National Heart, Lung, and Blood Institute; by grants UL1-TR-000040 and UL1-TR-001079 from the National Center for Research Resources National Institutes of Health Intramural Research Program, and by a grant from Bayer Healthcare for the use of the gadolinium contrast agent.

Disclosures

None.

Supplemental Material

Table S1–S3
References 61–75

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SUPPLEMENTAL MATERIAL

Table S1. Multivariable Association Between Baseline Assessment of Periodontal Disease and T1-Mapping Measures (Native T1 Mapping and Extracellular Volume Fraction) in Men after adjustment for co-variates from baseline examination

Men				
Regression Models	ECV (%)		Native T 1 (ms)	
	B± SE	P-value	B± SE	P-value
Model 1	0.6 ± 0.2	0.02	3.1 ± 3.2	0.3
Model 2	0.5 ± 0.2	0.02	2.0 ± 3.2	0.5
Model 3	0.6 ±0.2	0.01	1.8 ± 3.3	0.6

Model 1: Adjusted for age, race, body mass index

Model 2: Adjusted for variables included in model 1, lipid-lowering therapy, low-density lipoprotein, systolic and diastolic blood pressure, any hypertensive medication, diabetes status, education, income, smoking status, estimate glomerular filtration rate, left ventricular mass index, history of myocardial infarction

Model 3: Adjusted for variables included in model 2, except the substituted history of myocardial infarction with total angaston calcium score

Table S2. Multivariable Association Between Baseline Assessment of Periodontal Disease and T1-Mapping Measures (Native T1 Mapping and Extracellular Volume Fraction) in Women after adjustment for co-variates from baseline examination

Women				
Regression Models	**ECV (%)**		**Native T 1 (ms)**	
	B± SE	P-value	B± SE	P-value
Model 1	-0.2 ±0.2	0.4	6.3 ± 4.1	0.1
Model 2	-0.3 ±0.2	0.3	3.2 ± 4.2	0.4
Model 3	-0.3 ± 0.26	0.3	3.2 ± 4.2	0.4

Model 1: Adjusted for age, race, body mass index
Model 2: Adjusted for variables included in model 1, lipid-lowering therapy, low-density lipoprotein, systolic and diastolic blood pressure, any hypertensive medication, diabetes status, education, income, smoking status, estimate glomerular filtration rate, left ventricular mass index, history of myocardial infarction
Model 3: Adjusted for variables included in model 2, except the substituted history of myocardial infarction with total angaston calcium score

Table S3. Common Causes of Elevated Extracellular Volume

Common Causes of Elevated ECV		
Cardiac specific pathologies	**Infiltrative**	**Other**
Acute and chronic myocardial infarction [60,61]	Amyloidosis (light chain and transthyretin)[62]	Female sex [20]
Myocarditis[63]		Ageing [20,60]
Heart failure (both preserved and reduced ejection fraction)[64]		Rheumatological disorders [65-68]
Valvular disorders [69-71]		Smoking [72]
Ischemic and non-ischemic cardiomyopathy[73]		Diabetes [74]
Myocarditis[63]		Obesity [75]
		Inflammation (Interlukin-6 and c-reactive protein) [21]