Inflammatory Markers and Calcification of Coronary Arteries, Aorta, and Cardiac Valves in Older Adults: Findings from the Atherosclerosis Risk in Communities (ARIC) Study

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BACKGROUND

- Inflammation plays an important role in the pathophysiology of atherosclerosis
- Inflammatory biomarkers have been weakly associated with coronary artery calcium (CAC), a representative measure of subclinical atherosclerosis
- Existing evidence does not sufficiently explore extra coronary calcium (ECC) in this context even though a growing body of literature reports the additional prognostic value of ECC beyond CAC
- Different vascular beds may have differing pathophysiological mechanisms

STUDY OBJECTIVE

- To characterize the association of two inflammatory markers, high-sensitivity C-reactive protein (hs-CRP) and galectin-3, at middle age with CAC and ECC at older age in the community

METHODS

- The ARIC study is a **prospective cohort** of 15,792 participants aged 45 – 64 years at the baseline (visit 1,1987-1989).
- Cardiac CT performed among **1,934** ARIC participants without coronary heart disease at visit 7 (2018 - 2019)
- Serum hs-CRP and galectin-3 were measured at visit 4 (1996-1998)
- We examined the associations of hs-CRP and galectin-3 at visit 4 by **quartile** with presence of CAC and ECC (Agatston score >0 vs 0) at visit 7 using **multivariable logistic regression.**
- **Subgroup analyses** were performed for age, race, and sex.

RESULTS

Table 1. Baseline characteristics by quartile of hs-CRP and galectin-3 at visit 4, N = 1934

Variable*	hs-CRP (mg/L)				Galectin-3 (ng/mL)				
	Quartile 1 [0.2 – 1.0] (N = 477)	Quartile 2 [1.0 – 2.1] (N = 484)	Quartile 3 [2.1 – 4.7] (N = 488)	Quartile 4 [4.7 – 44.0] (N = 485)	Quartile 1 [5.1 – 11.6] (N = 499)	Quartile 2 [11.6 – 13.7] (N = 490)	Quartile 3 [13.7 – 15.9] (N = 468)	Quartile 4 [15.9 – 32.7] (N = 477)	Overall (N = 1934)
Age, years	58.9 [4.1]	59.6 [4.3]	59.2 [4.1]	59.0 [4.3]	59.0 [4.0]	59.1 [4.4]	59.4 [4.4]	59.3 [4.2]	59.2 [4.2]
Male	51%	45%	34%	21%	55%	44%	32%	19%	38%
White	84%	85%	82%	66%	82%	79%	81%	73%	79%
Current smoker	8%	10%	12%	10%	9%	11%	9%	11%	10%
Former smoker	47%	45%	41%	38%	46%	45%	43%	38%	43%
BMI (kg/m^2)	25.6 [3.6]	27.8 [4.1]	28.8 [4.7]	31.1 [6.1]	27.8 [4.6]	27.8 [4.9]	28.1 [4.9]	29.7 [5.8]	28.3 [5.1]
Diabetes	5%	5%	27 (5.5%)	12%	8%	6%	6%	8%	7%
Total cholesterol, (mmol/L)	5.1 [0.9]	5.2 [0.9]	5.2 [0.9]	5.2 [0.89]	5.1 [0.89]	5.2 [0.80]	5.3 [0.95]	5.21 [0.93]	5.18 [0.90]
HDL cholesterol, (mmol/L)	1.4 [0.4]	1.3 [0.4]	1.4 [0.4]	1.4 [0.44]	1.3 [4.07]	1.4 [0.43]	1.4 [0.44]	1.39 [0.43]	1.36 [0.43]
Statin use	6%	7%	7%	4%	5%	5%	8%	7%	6%
History of stroke	1%	0.2%	1%	2%	1%	1%	1%	1%)	1%
SBP	118 [14.8]	121 [16.4]	122 [15.9]	125 [17.5]	120 [14.8]	122 [17.2]	121 [15.8]	123 [17.5]	122 [16.4]
Anti-HTN med use	20%	24%	28%	40%	22%	27%	25%	37%	28%

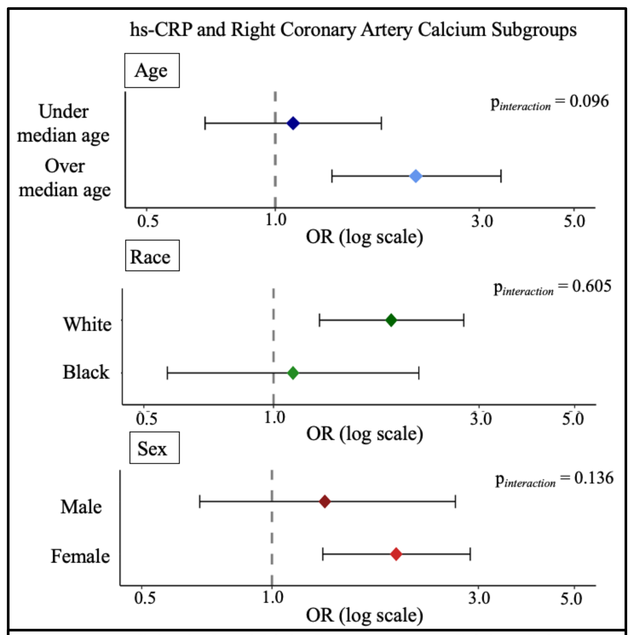

Table 2. Odds ratios (95% CI) of the presence of CAC and ECC according to hs-CRP and galectin-3 adjusted for all variables in Table 1 and ARIC center.

		hs-CRP	Galectin-3
		Highest vs. lowest quartile	Highest vs. lowest quartile
		OR (95% CI)	OR (95% CI)
Ascending Aorta	Unadjusted	**2.19 (1.62 – 2.99)**	1.33 (0.99 – 1.78)
	Adjusted	**1.45 (1.02 – 2.07)**	0.94 (0.68 – 1.30)
Descending Aorta	Unadjusted	0.85 (0.57 – 1.26)	1.27 (0.86 – 1.87)
	Adjusted	0.86 (0.53 – 1.41)	1.23 (0.80 – 1.91)
Aortic Valve Ring	Unadjusted	**1.62 (1.15 – 2.31)**	0.89 (0.63 - 1.27)
	Adjusted	1.47 (0.97 – 2.24)	0.82 (0.55 – 1.20)
Aortic Valve	Unadjusted	0.93 (0.72 – 1.20)	0.92 (0.72 – 1.19)
	Adjusted	1.08 (0.80 – 1.46)	1.11 (0.84 – 1.47)
Mitral Valve	Unadjusted	**1.55 (1.20 – 2.00)**	**1.43 (1.12 – 1.85)**
	Adjusted	1.14 (0.85 – 1.54)	1.19 (0.90 – 1.57)
Overall Coronary	Unadjusted	2.02 (0.91 – 2.02)	0.89 (0.59 – 1.34)
	Adjusted	1.20 (0.73 – 1.97)	1.08 (0.69 – 1.72)
Left Main	Unadjusted	1.23 (0.95 – 1.58)	0.94 (0.73 – 1.21)
	Adjusted	1.33 (0.99 – 1.81)	1.08 (0.82 – 1.43)
Left Anterior Descending	Unadjusted	1.14 (0.82 – 1.58)	0.80 (0.57 – 1.11)
	Adjusted	1.25 (0.84 – 1.87)	1.07 (0.74 – 1.55)
Left Circumflex	Unadjusted	1.19 (0.92 – 1.54)	0.79 (0.61 – 1.02)
	Adjusted	1.26 (0.92 – 1.74)	0.97 (0.73 – 1.31)
Right Coronary Artery	Unadjusted	**1.41 (1.08 – 1.84)**	1.12 (0.86 – 1.47)
	Adjusted	**1.55 (1.12 – 2.16)**	**1.48 (1.10 – 2.01)**

CONCLUSIONS

- Both hs-CRP and galectin-3 were associated with calcification of some (ex. ascending aorta and right coronary artery) but not all vascular beds tested
- Associations were generally consistent in demographic subgroups
- Suggests potentially unique atherosclerotic pathophysiology across different vascular beds
- Robust associations of inflammatory markers with right coronary artery calcification deserve further investigation

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