Title: History of Coronary Artery Disease and successful Revascularization Influences Coronary Microvascular Dysfunction (CMD), Anginal Presentation and Acute Cardiac Outcomes Among Patients with Non-Obstructive Coronary Artery Disease (No-CAD)

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Introduction: Up to 70% of the 1 million annual coronary angiographies in the U.S. reveal angina with non-obstructive coronary artery disease (ANOCA/INOCA). Coronary microvascular and vasomotor dysfunction (CMVD) is the primary mechanism of angina and ischemia in ANOCA patients and is associated with a high prevalence of CMD events, including endothelial-dependent dysfunction, microvascular spasm, and impaired coronary flow reserve. A subset of No-CAD patients, despite successful revascularization, continue to report angina, suggesting a persistent CMVD component. In this study, we compare clinical characteristics, CMVD profiles, anginal presentation, and acute cardiac outcomes between No-CAD patients with a history of obstructive CAD and successful revascularization (No-CAD with prior CAD) and those without any history of obstructive CAD (No-CAD without prior CAD).

Methods: No-CAD patients (<50% stenosis) were divided based on history of obstructive disease: no prior obstructive disease versus prior PCI with ≤50% residual stenosis or >50% stenosis with negative FFR. This retrospective cohort study used EMR data from October 2020 to December 2024 for patients with angina and non-obstructive CAD confirmed by LHC (≤50% stenosis or >50% with negative FFR in LAD, LCX, RCA). Patients with prior CABG or a primary diagnosis of MINOCA were excluded. ICFT was performed using Doppler or bolus thermodilution methods assessing both endothelial-dependent and -independent coronary dysfunction. CMD events including elevated index of microcirculatory resistance (IMR > 25), reduced coronary flow reserve (CFR < 2.0), endothelial-dependent and independent dysfunction, and abnormal responses to acetylcholine (ACH) were collected over one year following ICFT through electronic medical record review.

Results: Among 350 patients with No-CAD, 60 (17%) had prior obstructive CAD and PCI. Those with a history of prior CAD had higher rates of male sex (p<0.001), hypertension (p<0.001), hyperlipidemia (p=0.045), type 2 diabetes (p<0.001), atrial fibrillation (p=0.015), and cerebrovascular events (p=0.032). Anginal burden was significantly higher among patients with prior CAD, as reflected by lower SAQ-7 scores (median 18.6 vs 33.3, p=0.002), though CCS and NYHA functional class distributions were similar. There was no significant difference in endothelial-dependent dysfunction (p=0.193) or microvascular spasm between groups (p=1.00). Additionally, CFR and IMR values were comparable between groups (p=0.279 and p=0.067, respectively), and elevated IMR >25 was observed only in patients without prior CAD (15% vs 0%, p=0.126).

Conclusion: In patients with non-obstructive coronary artery disease, a history of prior obstructive CAD and revascularization is associated with greater anginal burden and a higher prevalence of cardiovascular risk factors, despite similar coronary microvascular dysfunction profiles and CMD event prevalence.

Table 1. Results	No CAD (N=350)	History of CAD (N=60)	P-value
Demographics			
Age in Years, Median (IQR)	56 (47, 66)	60 (52, 68)	0.096
Female, N (%)	315 (90)	42 (70)	<0.001
Race/Ethnicity, N (%) **White** **Black** **Hispanic**	 296 (86) 37 (11) 7 (2)	 48 (81) 10 (17) 1 (2)	0.543 1.00
BMI, kg/m^2 , Median (IQR)	29.3 (25.5, 35.6)	29.5 (25.7, 36.0)	0.705
Clinical Characteristics			
Hypertension, (N, %)	190 (54)	47 (78)	<0.001
Hyperlipidemia, (N, %)	269 (77)	53 (88)	0.045
Type 2 Diabetes, (N, %)	43 (12)	25 (42)	<0.001
Heart failure with preserved ejection fraction (HFpEF), N (%)	26 (7)	7 (12)	0.265
Heart failure with preserved ejection fraction (HFrEF), N (%)	6 (2)	3 (5)	0.131
Atrial Fibrillation	25 (7)	10 (17)	0.015
History of Myocardial Infraction d/t obstructive CAD	0 (0)	3 (16)	0.002
History of Cerebrovascular Event (CVA)	24 (7)	9 (15)	0.032
Validated Questionnaire Scores			
Vasospastic Angina (N,%)	60 (17)	5 (8)	0.340
Microvascular Angina (N,%)	71 (20)	14 (23)	0.340
Duke Activity Status Index (DASI), Median (IQR)	32.0 (20.5, 44.5)	28.5 (20.8, 42.5)	0.535
Seattle Angina Questionnaire SAQ-7, Median (IQR)	33.3 (18.6, 48.6)	18.6 (6.1, 39.4)	0.002
University of California Shortness of Breath Scale (UCSD-SOB), Median (IQR)	37 (22, 58)	47 (22, 73)	0.150
Perceived Stress Scale (PSS), Mean ± SD	14.0 ± 6.3	16.0 ± 7.7	0.063
CMD Diagnosis			
ICFT Method **Doppler (%)** **Thermodilution (%)**	 229 (65) 121 (35)	 31 (52) 29 (48)	0.041
Change in CD, Median (IQR)	-0.042 (-0.099, 0.023)	-0.027 (-0.081, 0.035)	0.436
Coronary Flow reserve, Median, (IQR)	2.2 (1.8, 2.7)	1.9 (1.6, 2.4)	0.279
Change in CBF %, Median (IQR)	0.20 (0.06, 0.69)	0.17 ((0.06, 0.59)	0.894
Endothelial Independent CMD, N (%)	56 (17)	10 (21)	0.510
Endothelial Dependent CMD, N(%)	148 (42)	20 (33)	0.193
Epicardial Spasm, N (%)	19 (5)	7 (12)	0.067
Mixed Disease	137 (39)	21 (35)	0.542