

Age Differences in Coronary Microvascular Dysfunction Presentation in Patients with Angina with Non-Obstructive Coronary Arteries (ANOCA)

Jane Carnesi; Danielle Tapp, PhD; Namrita Ashokprabhu, BS; Christian Schmidt, MS; Paxson Tipler, MS; Claire Hanycz; Evan Lahkia; Kaiya Hansen, MS2; Isabella Duke-Ibanez; Michelle Hamstra, MS; Timothy D. Henry, MD, Odayme Quesada MD

Background

- Up to 50% of patients undergoing coronary angiography for evaluation of stable angina will have no evidence of obstructive disease, known as Angina with No Obstructive Coronary Artery Disease (ANOCA)
- Coronary Microvascular Dysfunction (CMD) is thought to be the primary pathophysiological mechanism of ANOCA
- CMD can be tested via invasive coronary functional angiography (CFA) presenting as three primary endotypes: endothelial dependent, endothelial independent and epicardial spasm
- While ANOCA patients tend to be younger than patients with obstructive coronary artery disease, there are limited studies surrounding the influence of age on CMD presentation in ANOCA

Objective

Compare differences in CMD diagnosis and angina presentation across three age groups of ANOCA patients

Methods

- ANOCA (<50% stenosis in coronary arteries) patients that underwent invasive CFA were divided into three age groups: less than 45 (<45), between 45 and 55 (45-55), and over 55 (>55)
- Clinical characteristics, anginal presentation, and validated questionnaires were collected as described in Table 1
- CMD diagnoses and continuous measures were categorized as the following:
 - Endothelial-independent CMD (coronary flow reserve [CFR] < 2.5 in response to adenosine)
 - Endothelial-dependent CMD (coronary blood flow [CBF] < 50% or no change in vessel diameter in response to 54mcg intracoronary acetylcholine)
 - Epicardial spasm (>90% constriction) to 108 mcg intracoronary acetylcholine

Results

Table 1. Results	<45 Years (N=54)	45-55 Years (N=82)	>55 Years (N=165)	P-value (Main Effect)
Demographics				
Age (Mean, ±SD)	37.2 ± 5.2 †^	50.5 ± 3.3 † ‡	65.6 ± 6.3 †^	<0.001
Sex (N, %)				
M	5 (9)	5 (6)	12 (7)	0.769
F	48 (91)	77 (94)	151 (93)	
Hypertension (N, %)	27 (50)^	50 (61)	119 (72)^	0.008
Diabetes (N, %)	2 (4) ‡	16 (20) ‡	25 (15)	0.032
Angina Presentation and Validated Questionnaires				
CCS Class (N, %)				
1	10 (34)	15 (28)	41 (41)	0.290
2	4 (14)	9 (17)	23 (23)	
3	11 (38)	22 (41)	23 (23)	
4	4 (14)	8 (15)	13 (13)	
SAQ7 ¹ (Median, IQR)	29.2 (18.8, 40.1)^	33.3 (16.1, 45.8)	37.1 (23.3, 54.2)^	0.033
DASI ¹ (N, Mean, SD)	41.0 ± 13.2^	37.4 ± 12.6 ‡	29.0 ± 12.4^ ‡	<0.001
UCSD SOB ² (Median, IQR)	37 (22, 50)	35 (23, 53)	34.5 (15, 57)	0.924
Vasospastic Angina (N, %)	48 (89)^	73 (89) ‡	125 (76) ^ ‡	0.013
Microvascular Angina (N, %)	42 (78)	70 (85)	144 (87)	0.235
CFA Results				
Endothelial Dependent CMD (N, %)	25 (45) †^	55 (71) ‡	93 (59)^	0.018
Endothelial Independent CMD (N, %)	25 (51)^	46 (59)	106 (69)^	0.048
Coronary Flow Reserve (Median, IQR)	2.5 (2.0, 2.9)^	2.35 (1.8, 2.8)	2.1 (1.7, 2.6)^	0.007
% Change CBF (Median, IQR)	0.83 (.36, 1.03) †^	0.11 (-0.16, .65) † ‡	0.20 (0.08, 0.69) †^	<0.001
% Change in Vessel Diameter (Median, IQR)	4.4 (-5.5, 14.1) †^	-7.2 (-12.6, -2.8) † ‡	-1.8 (-7.6, 3.3) †^	<0.001
Epicardial Spasm (N, %)	14 (26)	24 (29)	44 (27)	0.885
Any Abnormal CFA Finding (N, %)	40 (74) †^	73 (89) ‡	145 (88)^	0.025

Comparisons were made via chi-square for proportions (%), one way ANOVA (mean, SD) or one way ANOVA on ranks for non-normally distributed data (median, IQR). Post-hoc testing (Tukey's) was conducted for pairwise comparisons. CSS: Canadian Cardiovascular Society Angina Grade, DASI: Duke Activity Status Index; UCSD SOB: University of San Diego Shortness of Breath; SAQ7: Seattle Angina Questionnaire; PSS¹ indicates higher scores associated with better quality of life/function; life; ² Higher scores = worse functionality/quality of life; Interquartile Range (IQR); Standard Deviation (SD)

For Pairwise Comparisons:

‡ denotes a significant difference (p<0.05) between <45 and 45-55
 † denotes a significant difference (p<0.05) between <45 and 55+
 ^ denotes a significant difference (p<0.05) between 45-55 and 55+

Results (Continued)

- ANOCA patients <45 years had a lower prevalence of hypertension compared to patients >55 and a lower prevalence of diabetes to 45-55
- Patients <45 had lower SAQ-7 scores compared to the 55+ group, indicating worse anginal severity/quality of life. Yet, DASI scores were higher in patients <45 and in patients 45-55 compared to >55, suggesting decreased functional with age capacity
- Patients <45 and 45-55 had a higher prevalence of vasospastic angina compared to older patients 55+
- Abnormal CFA findings were less prevalent in patients <45 compared to patients >55, with lower prevalence of endothelial dependent CMD and endothelial independent CMD
- CFR was lower in both the <45 and 45-55 age groups compared to >55, Change in %CBF was greatest in patients <45 compared to other groups, % change in vessel diameter was highest in patients <45

Conclusions

- Younger ANOCA patients (<45 and 45-55) had a higher prevalence of vasospastic, or random chest pain, compared to older patients
- Functional capacity measured by DASI decreased with age, consistent with prior literature. In contrast, SAQ-7 decreased with age suggesting worse anginal scores in younger patients. This may be due to limitations of the SAQ.
- Younger patients were less likely to display abnormal CFA findings, which was supported by the lower prevalence of endothelial dependent and independent CMD in patients <45
- These results highlight the potential for age as a risk factor for CMVD endotypes in ANOCA patients, though further study is needed to establish these effects



Table 1. Results	<45 Years (N=54)	45-55 Years (N=82)	>55 Years (N=165)	P-value (Main Effect)
Demographics				
Age (Mean, ±SD)	37.2 ± 5.2 †^	50.5 ± 3.3† †	65.6 ± 6.3†^	<0.001
Sex (N, %)				
M	5 (9)	5 (6)	12 (7)	
F	48 (91)	77 (94)	151 (93)	0.769
Hypertension (N, %)	27 (50)^	50 (61)	119 (72)^	0.008
Diabetes (N, %)	2 (4) †	16 (20) †	25 (15)	0.032
Angina Presentation and Validated Questionnaires				
CCS Class (N, %)				
1	10 (34)	15 (28)	41 (41)	
2	4 (14)	9 (17)	23 (23)	0.290
3	11 (38)	22 (41)	23 (23)	
4	4 (14)	8 (15)	13 (13)	
SAQ7 † (Median, IQR)	29.2 (18.8, 40.1)^	33.3 (16.1, 45.8)	37.1 (23.3, 54.2)^	0.033
DASI † (N, Mean, SD)	41.0 ± 13.2^	37.4 ± 12.6†	29.0 ± 12.4^†	<0.001
UCSD SOB ‡ (Median, IQR)	37 (22, 50)	35 (23, 53)	34.5 (15, 57)	0.924
Vasospastic Angina (N, %)	48 (89)^	73 (89) †	125 (76) ^†	0.013
Microvascular Angina (N, %)	42 (78)	70 (85)	144 (87)	0.235
CFA Results				
Endothelial Dependent CMD (N, %)	25 (45) †^	55 (71) †	93 (59)^	0.016
Endothelial Independent CMD (N, %)	25 (51)^	46 (59)	106 (69)^	0.046
Coronary Flow Reserve (Median, IQR)	2.5 (2.0, 2.9)^ N=37	2.35 (1.8, 2.8) N=64	2.1 (1.7, 2.6)^ N=119	0.007
% Change CBF (Median, IQR)	0.83 (.36, 1.03)†^ N=23	0.11 (-0.16, .65)††	0.20 (0.08, 0.69) †^	<0.001
% Change in Vessel Diameter (Median, IQR)	4.4 (-5.5, 14.1) †^	-7.2 (-12.6, -2.8) ††	-1.8 (-7.6, 3.3) †^	<0.001
Epicardial Spasm (N, %)	14 (26)	24 (29)	44 (27)	0.885
Any Abnormal CFA Finding (N, %)	40 (74) †^	73 (89) †	145 (88)^	0.025