Assessment of Clinical Presentation for Patients with Angina and Non-Obstructive Coronary Artery Disease and a History of Adverse Pregnancy Outcomes

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

The Christ Hospital Health Network
Women's Heart Center

Background

- Angina without obstructive coronary arteries (**ANOCA**) affects 3 to 4 million individuals in the US, **70%** of which are **women**
- Adverse pregnancy outcomes (APO) complicate roughly 30% of all pregnancies and are an increasingly recognized risk factor for cardiovascular diseases
- History of APO is associated with **two-fold higher odds** of cardiovascular disease and adverse cardiac remodeling up to 10 years following pregnancy
- Coronary microvascular dysfunction (**CMD)** is the predominant pathophysiology underlying ANOCA, and CMD in a pregnant population is linked to a 30% increased risk of APO development
- How APOs affect angina presentation and CMD diagnosis in a cohort of ANOCA patients compared to ANOCA patients with normotensive pregnancy (NTP) history remains unknown

Objective

To compare clinical characteristics, angina symptoms, and coronary microvascular dysfunction (CMD) prevalence between patients with ANOCA/INOCA and a history of APO

Methods

- A (2020-2024) prospective registry-based cohort study of ANOCA patients (<50% stenosis in any major epicardial artery) with a history of one or more pregnancies that underwent invasive coronary functional angiography (CFA) for diagnosis of CMD
- APO categories included Gestational Diabetes (Gest DM), Preterm Birth, Gestational Hypertension (Gest. HTN), Preeclampsia, Eclampsia, and HELP Syndrome (**Table 1**, Angina characteristics compared as described in **Table 2**)
- CFA diagnoses 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. Clinical and Pregnancy Characteristics

	ANOCA with History of NTP (ANOCA hx NTP) N=482	ANOCA with History of APO (ANOCA hx APO) N=199	P-Value
Clinical Characteristics and Demographics			
Age, Median (IQR)	62 (53, 69)	52 (43, 62)	**<0.001**
Race/Ethnicity, N (%)			
White	458 (85)	125 (87)	0.489
Black	53 (10)	15 (10)	0.821
Hispanic/Latino	9 (2)	4 (3)	0.489
Hypertension, N (%)	344 (64)	106 (74)	**0.022**
Hyperlipidemia, N (%)	494 (92)	127 (89)	0.259
BMI, Median (IQR)	28.8 (24.6, 34.1)	32.0 (26.8, 37.9)	**<0.001**
Refractory Angina (N, %)	98 (20)	39 (20)	0.828
Diabetes (N, %)	73 (15)	46 (23)	**0.013**
Pregnancy Characteristics			
Years from last Pregnancy To CFA, Median (IQR)	33.1 (22.6, 40.7)	22.1 (12.5, 30.0)	**<0.001**
Parity, N (%)			
1	116 (22)	34 (24)	0.790
2	214 (40)	53 (37)	
3+	208 (39)	56 (39)	
APO Type (N, %)			
Gest DM		67 (34)	
Preterm Birth		37 (19)	
Gest. HTN		76 (38)	N/A
Preeclampsia		88 (44)	
Eclampsia		5 (3)	
HELP		4 (2)	

Table 2. Angina Presentation and CFA Results

	ANOCA with History of NTP (ANOCA hx NTP) N=482	ANOCA with History of APO (ANOCA hx APO) N=199	P-Value
Validated Questionnaires and Angina Presentation			
CCS Class, N (%)			
1	123 (44)	37 (31)	0.088
2	72 (26)	36 (30)	
3	62 (22)	29 (24)	
4	25 (9)	17 (14)	
SAQ-7, Median (IQR)	45.8 (29.2, 60.0)	40.8 (23.9, 55.8)	**0.045**
PSS, Median (IQR)	12 (8.5, 17)	13 (10, 18)	**0.011**
DASI, Median (IQR)	35.3 (24, 45.3)	34.8 (23.1, 46.5)	0.814
UCSD SOB, Median (IQR)	26 (9, 47)	27.5 (11.5, 53.5)	0.182
Vasospastic Angina, N (%)	361 (75)	151 (76)	0.787
Microvascular Angina, N (%)	371 (77)	156 (78)	0.687
CFA Results			
CRT Performed, N (%)	141 (29)	72 (36)	0.076
Endothelial Dependent CMD, N (%)	72 (58)	29 (46)	0.119
Endothelial Independent CMD,N (%)	84 (65)	39 (64)	0.927
Epicardial Spasm, N (%)	48 (34)	22 (31)	0.608
Any Abnormal CRT Finding, N (%)	125 (89)	59 (82)	0.177
CFR, Median (IQR)	2.0 (1.8, 2.6)	2.3 (2.0, 2.7)	0.093
% Change CBF, Median (IQR)	0.18 (0.02, 0.74)	0.29 (0.08, 0.66)	0.666
% Change in Vessel diameter, Mean (SD)	-0.04 (0.12)	-0.02 (0.15)	0.540

IQR: Interquartile Range; CSS: Canadian Cardiovascular Society Angina Grade, DASI: Duke Activity Status Index; USCD SOB: University of San Diego Shortness of Breath; SAQ7: Seattle Angina Questionnaire; PSS: Perceived Stress Score; CFR: Coronary Flow Reserve; CBF: Coronary Blood Flow

Results (Continued)

- A total of 199 ANOCA patients had a history of APO (ANOCA hx APO), and 482 patients had a history of NTP (ANOCA hx NTP)
- Patients with a history of APO were **younger** (Median age =52, p<0.001) and presented earlier from their last pregnancy to CFA (p<0.001, Table 1)
- ANOCA patients with a history of APO had **higher** BMI (mean=32, P=0.001), had a **higher** prevalence of hypertension (74%,P=0.022), and had a **higher** prevalence of diabetes (23%, P=0.013) compared to ANOCA hx NTP (Table 1)
- ANOCA hx APO had lower SAQ-7 scores (Median= 40.8) compared to NTP (Median=45.8), consistent with more **severe angina** (P= 0.045, Table 2)
- ANOCA hx APO had **higher perceived stress** score using the PSS questionnaire (Median= 13) compared to ANOCA hx NTP (Median=12, P=0.011, Table 2)
- There were no significant differences between the groups CFA diagnoses, prevalence of abnormal CFA finding or continuous measures of CMD (Table 2)

Conclusions

- ANOCA patients with a history of APO were younger and presented earlier to CFA compared to patients with a history of NTP
- Additionally, ANOCA patients with a history of APO presented with a higher rate of cardiovascular risk factors compared to NTP
- ANOCA patients with a history of APO demonstrated worse angina and higher levels of perceived stress compared to those with a history of NTP which suggests a lower quality of life.
- Despite anginal differences, there were no differences in underlying CMD presentation between these groups
- These results suggest that history of APO is a risk factor for worse anginal symptoms in ANOCA
- Further study is needed to discern the relationship between specific APO and time since pregnancy on anginal presentation in women with ANOCA

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Contact PI: **Odayme Quesada, MD** (Odayme.quesada@thechristhospital.com)

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