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Original article

Evaluation of the Cardiovascular Risk in Women With PCOS

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Abstract:

Background: Evaluation of the cardiovascular (CV) risk in a sample of CV asymptomatic infertile women with polycystic ovary syndrome (PCOS). **Methods**: 100 infertile PCOS women older than 30 years (PCOS group) and 50 fertile non-PCOS women (Non-PCOS group) underwent gynecological and laboratory diagnosis. The diagnostic protocol included determination of body mass index (BMI), Homeostasis model assessment of insulin resistance (HOMA-IR) scoring and cardiologic evaluation using echocardiography, estimation of carotid artery intima-media thickness (CIMT), coronary artery calcium (CAC) score using multi slice non-contrast cardiac CT and cardiac risk ratio (CRR). Study outcomes included the incidence of abnormal cardiac risk parameters and determination of the best minimally invasive modality to be used as screening test. **Results:** The median values of CRR, CIMT and CAC Agatson score were significantly higher among PCOS women than in Non-PCOS women. Estimated cardiac risk parameters were positively correlated with the level of hyperandrogenemia, BMI, and HOMA-IR score. High CRR was found to be the most important predictor for the risk of atherosclerosis as judged by CIMT and CIMT was the most important predictor for the risk of coronary atherosclerosis as judged by CAC score. Statistical analyses defined high BMI and CIMT as the sensitive significant predictors for high CAC score. **Conclusion**: Adult cardiac asymptomatic PCOS women had high cardiovascular risk. Estimation of CRR is non-invasive, cheap and available screening tool and had predictive ability to detect women had high CIMT. CIMT is a minimally invasive predictor for the extent CAC.

Keywords: Cardiovascular risk, Polycystic Ovary Syndrome, Infertility, Cardiac risk ratio, Carotid intima-media thickness.

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Introduction

Polycystic ovary syndrome (PCOS) is a widespread endocrine and metabolic disorder which affects both adult and adulthood women (1) and is associated with menstrual irregularity, hyper-androgenism, and infertility among women of childbearing period (2). PCOS in adolescents is associated with adiposity, higher androgen concentrations and greater menstrual irregularity, in youth PCOS is considered a risk factor for type 2 diabetes mellitus in adulthood (3) and confers an increased risk of cardiometabolic disease in later life (4).

Early identification and treatment of cardiovascular disease risk factors through screening of apparently healthy individuals is crucial for the primary prevention of cardiac insults (5). Carotid intima-media thickness (CIMT), plaque quantification and coronary artery calcium (CAC) scoring have an important role in preventative cardiology to improve cardiovascular risk prediction especially for asymptomatic individuals classified as low-to-intermediate risk (6).

The CIMT is a feature of vascular endothelial inflammatory response leading to gradual trans-differentiation of endothelial cells to adopt the phenotypic characteristics of mesenchymal cells (7). Thickening of intima-media appears in a long subclinical period of atherosclerosis and IMT was found to correlate with atherosclerotic deterioration of the arterial wall in other vascular territories and with cardiovascular events (8). The IMT was defined as wall thickness of >0.9 mm, while focal thickening of ≥1.5 mm that protrudes into the lumen as asymptomatic carotid plaque increases the risk of cardiac events from 16 to 36% in cardiac asymptomatic patients (9).

The coronary artery calcium (CAC) score is powerful discriminator of cardiovascular risk (10) and was measured using a 16-channel computed tomographic system and reported as an Agatston score, to provide a snapshot of atherosclerotic burden (11). CAC score =0 has a very low future event rate, while non-zero CAC scores are associated with a progressive, graded increase in risk with increased CAC score (12). Moreover, CAC=0 was indicator of a favorable long-term prognosis of adults aged ≤55 years, particularly among nonsmokers (10).

Objectives

The present study aimed to evaluate the cardiovascular (CV) risk in a sample of CV asymptomatic infertile PCOS women who are aged >30 years old.

Design:

Prospective observational comparative study

Setting:

Departments of Cardiology, and Internal Medicine, Faculty of Medicine, Tanta and Benha Universities

Ethical consideration

The study protocol was approved by the Local Ethical Committee, Faculty of Medicine, Tanta University (Approval code: 35179/1/22) and was registered at ClinicalTrials.gov. by number NCT05344547.

Patients & Methods

Women attending the infertility clinics at Tanta and Benha University Hospitals from Feb 2022 till Sep 2022 were eligible for evaluation for the PCOS as a cause of infertility. Gynecological evaluation entails data concerning present and past history of menstrual regularity, previous pregnancy for married women, previous investigations or therapies for PCOS or infertility. PCOS was diagnosed depending on the presence of at least two of the Rotterdam criteria (13, 14). Then, PCOS women fulfilling the inclusion criteria were referred for the concerned outpatient clinics for evaluation of the study parameters which include the following items:

1. Body mass index (BMI): was calculated and graded according to WHO guidelines (15, 16).
2. Insulin resistance (IR) was evaluated using the homeostasis model assessment of IR (HOMA-IR) score with a score of >2 is considered abnormal (17).
3. Cardiac evaluation
   - History taking history of previous acute cardiac attack, hypertension, and manifestations of heart failure, chronic kidney disease, or maintenance of antihypertensive therapy must be inquired about.
   - Clinical examination for the presence of any manifestation of congenital cardiac lesion, valve disease, vascular anomalies or diseases. Then, patients underwent complete cardiologic workup for evaluation of CV risk using the following investigations and scores:
     a. Doppler echocardiography was performed as previously (18) using an ultrasound system with image analysis by EchoPAC software (General Electric). The following parameters were estimated: left ventricular end diastolic (LVDd) and systolic (LVSd) diameters, the percentage

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of fractional shortening (FS%), left ventricular mass index, left atrial diameter (LAD), ejection fraction, deceleration time (DcT)

b. Carotid IMT was measured as previously described (19), using a longitudinal 2D B-mode image.
c. Coronary Artery Calcium (CAC) Score: CAC is quantified through multi slice non-contrast cardiac CT as previously described (20). Calcified coronaries were defined (21) and the CAC Agatston score was calculated (22).
d. Cardiac risk ratio (CRR) was calculated according to Genest et al. (23) as serum total cholesterol (TC) level divided by serum high-density lipoprotein-cholesterol (HDL-c) level and woman with CRR at ≥3.5 was considered at risk of cardiac disease (24).

Exclusion criteria

Age younger than 30 years old, BMI>35 kg/m^2, presence of acute or chronic inflammatory diseases, diabetes mellitus, hyperprolactinemia, thyroid dysfunction, Cushing's syndrome, congenital adrenal hyperplasia, adrenal tumor or ovarian tumor, autoimmune disease, malignancy, central nervous system disease, current or previous use of oral contraceptives within 6 months of enrollment were excluded from the study. Patients had congenital cardiac lesions, manifestations of hypertension especially unequal carotid pulse, neurological affection, renal diseases or family history of cardiac or cerebrovascular insults, ejection fraction <50%, regional wall motion abnormalities and significant valvular diseases were excluded.

Inclusion criteria and grouping

Infertile PCOS women older than 30 years and free of exclusion criteria were enrolled in the study as PCOS group. Fifty non-PCOS women of age- and BMI cross-matched to the enrolled PCOS women with regular menstrual cycles or fertile if married were collected as control (non-PCOS) group. Only women who signed the written informed consent will be enrolled in the study.

Laboratory investigations

Blood Sampling

All enrolled women were asked to attend the hospital lab fasting for 12 hours and gave blood sample for estimation of blood lipid profile and to re-attend on the 2nd day fasting for 8 hours to give another sample for estimation of fasting blood glucose and determination of hormonal profile levels. Blood samples were obtained under complete aseptic condition for estimation of blood glucose levels and serum levels of hormones and lipids.

Estimated parameters

1. Blood glucose levels were estimated by glucose oxidase method using BT1500 Automatic biochemistry analyzer (SPAN Diagnostics, Gujarat India).
2. Serum levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were estimated by photoluminescence methods using BT1500 Automatic biochemistry analyzer (SPAN Diagnostics, Gujarat India).
3. Serum levels of insulin, testosterone (T) and dehydroepiandrosterone sulfate (DHEA-S) using Automatic Immunoassay Analyzer (MAGLUMI 600, Snibe Diagnostic Co., Ltd., China).

Study outcomes

1. The primary outcome is the incidence of abnormal cardiac risk parameters among PCOS women who were apparently cardiac free women.
2. The secondary outcome is the best minimally invasive diagnostic approach to be used as screening test for these women.

Sample size calculation

Sample size calculation was based percent of difference in proportion of CAC>10 between PCOS and control groups as documented previously (25). Using G power calculator to calculate difference between 2 proportions using exact test with expected difference of 23.3%, 2-tailed, with α error =0.05 and power of 80%. The minimal calculated sample size was 84 PCOS women and 42 non-PCOS women as control group, and so as to get higher power, 100 PCOS women and 42 Non-PCOS women were recruited for the current study.

Statistical analysis

The results were analyzed using One-way ANOVA and Chi-square (X^2 test) test and the relation between the studied variate was studied using the Spearman's correlation analysis. The predictability of the studied variate for outcomes was evaluated using the Receiver Characteristic Curve and the Automatic Linear Modeling analyses using the IBM® SPSS® Statistics (Version 22, 2015; Armonk, USA). Significance of the results was determined at cutoff point of $P < 0.05$.

Results

The study included 135 infertile PCOS women, 35 were excluded for not fulfilling the inclusion criteria and 100 women were enrolled in the study (Fig. 1).

There were 37 single and 63 marries women and all were older than 30 years and had BMI<35 kg/m^2 with non-significant differences between PCOS and

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Non-PCOS women. All married control women were fertile, while among PCOS women, 53 women had primary and 10 had secondary infertility. All single control women had regular menstrual cycle free of abnormalities regarding duration or amount of bleeding, while 26 PCOS single women had oligomenorrhea and 11 had amenorrhea. Seventy –five women; 4 Non-PCOS and 71 PCOS women had ovarian volume >10 cm^3 with significantly higher frequency among the PCOS women with significantly median value of ovarian volume in comparison to Non-PCOS women (Table 1).

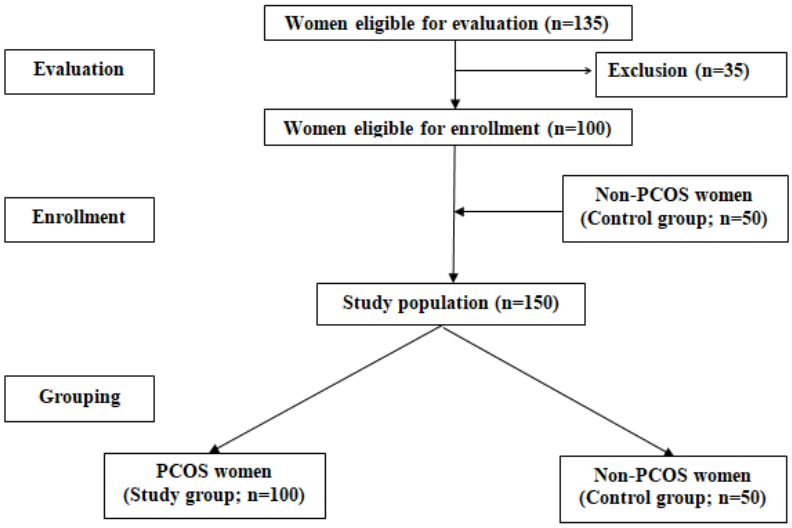

Fig. (1): Study Flow Chart

Table (1): Demographic and clinical data of study participants

Data		Group	Non-PCOS (n=50)	PCOS (n=100)	P value
Age (year)	Categories	30-35	27 (54%)	52 (52%)	0.418
		36-40	18 (36%)	24 (24%)	
		>40	5 (10%)	14 (14%)	
	Mean (±SD)		35.8 (±2.9)	36 (±3.3)	0.718
BMI (kg/m^2)	Overweight (25-29.9)		6 (12%)	10 (10%)	0.708
	Obese (30-34.9)		44 (88%)	90 (90%)	
	Mean (±SD)		32.1 (±1.5)	32.3 (±1.3)	0.378
Marital status	Married		29 (58%)	63 (63%)	0.553
	Single		21 (42%)	37 (37%)	
Fertility status of married women	Fertile		29 (100%)	0 (0%)	-
	Primary infertility		0	53 (77.9%)	
	Secondary infertility		0	10 (22.1%)	
Menstrual status of single women	Regular		21 (100%)	0 (0%)	-
	Oligomenorrhea		0	26 (70.3%)	
	Amenorrhea		0	11 (29.7%)	
Ovarian volume (mm^3)	<10		46 (92%)	29 (29%)	<0.001
	>10		4 (8%)	71 (71%)	
	Median volume [IQR]		6.75 [6.25-7.9]	10.95 [9.5-12.7]	<0.001
HOMA-IR score	Insulin resistant		5 (10%)	31 (31%)	<0.001
	Insulin sensitive		45 (90%)	69 (69%)	
	Median score [IQR]		0.42 [0.31-0.53]	1.4 [1.12-2.15]	<0.001

According to the calculated HOMA-IR score, 31 PCOS and 5 Non-PCOS were IR with significant difference regarding the frequency and median score. Seventy-two PCOS women were hyperandrogenemic with significant difference between both groups as regards the frequency and serum levels. Serum DHES, TC and TG levels were significantly higher, while serum HDL-c levels were significantly lower in PCOS than Non-PCOS women (Table 2).

All Non-PCOS and 10 PCOS women had CRR of <3.5 with significantly lower frequency of women had CRR of <3.5 and significantly higher median value among PCOS. The median value of estimated CIMT was significantly higher in PCOS women. Sixty seven women had CAC score of 0, 38 women had CAC score of <10 and 45 women had CAC score of >10 with significantly (p=0.008) higher distribution of PCOS women among higher CAC Agatson scores. Both calculated mean and median CAC Agatson score values were significantly (0.0005 & 0.0009, respectively) higher in PCOS women (Table 3)

Table (2): Laboratory data of the study participants

Data	Group		Non-PCOS (n=50)	PCOS (n=100)	P-value
HOMA-IR index	**Insulin sensitivity**	**Insulin resistant**	5 (10%)	31 (31%)	0.005
		Insulin sensitive	45 (90%)	69 (69%)	
	Median score [IQR]		0.42 [0.31-0.53]	1.4 [1.12-2.15]	<0.001
Serum testosterone	**Frequency of hyperandrogenemia**		0	72 (72%)	<0.001
	Mean (±SD) level		0.388±0.09	0.996±0.2	<0.001
Serum Dehydroepiandrosterone sulfate			14.8±2	24.1±5.1	<0.001
Total cholesterol (mg/dl)			160.9±9.6	183.7±17.7	<0.001
High-density lipoprotein cholesterol (mg/dl)			49.2±2.5	39.3±3.6	<0.001
Triglycerides (mg/dl)			51±8	82.9±11.3	<0.001
Low-density lipoprotein cholesterol (mg/dl)			60.7±6	61.5±14.9	0.351

Table (3): Cardiac risk data of the study participants

Data	Group		Non-PCOS (n=50)	PCOS (n=100)	P-value
CRR (TC/HDL)	**Frequency**	**<3.5**	50 (100%)	10 (10%)	<0.001
		≥3.5	0	90 (90%)*	
	Median [IQR]		3.33 [3.1775-3.39]	4.68 [4.35-5.2]*	<0.001
CIMT (mm)	**Median [IQR]**		0.44 [0.38-0.48]	0.485 [0.45-0.55]*	<0.001
CAC score	**Distribution of CAC Agatson Scores**	**0**	30 (60%)	37 (37%)	0.008
		<10	12 (24%)	26 (26%)	
		10-49	8 (16%)	23 (23%)	
		≥50	0	14 (14%)*	
	Mean (SD)		5.12±10.2	16.31±20.8*	0.0005
	Range		0-42	0-69	
	Median [IQR]		0 [0-6]	6.5 [0-26.75]*	0.0009

* indicates significant difference; p>0.05 indicates non-significant difference

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Estimated CIMT and CRR showed positive significant correlation with both ovarian size and serum testosterone levels, while CAC score showed positive significant correlation with serum testosterone levels. Regarding PCOS-metabolic disturbances, CAC score, CIMT and CRR were positively correlated with BMI in decreasing order of significance and both of CAC score and CIMT were positively correlated with HOMA-IR score. Only, CIMT showed positive significant correlation with age of PCOS women (Table 4).

Evaluation of the variables correlated with cardiac risk variables as predictors for the risk of atherosclerosis as judged by CIMT defined high CRR as the most important predictor for CIMT with predictive value of 33%, followed by older patients' age by 24%, ovarian size by 18%, high HOMA-IR score by 14% and hyperandrogenemia by 12% (Fig. 2). For prediction of coronary atherosclerosis and risk of oncoming cardiac events, high CIMT was the most important predictor by a value of 51%, followed by high BMI by 38% and high HOMA-IR score by 11% (Fig. 3).

Table (4): Spearman's correlation analysis between cardiac risk variables and PCOS-related endocrinal and metabolic disturbances in the studied PCOS women

Variables	CAC score		cITM		CRR	
	Rho.	P	Rho.	P	Rho.	P
Age	0.151	0.135	0.224	0.025	0.072	0.477
BMI	0.349	<0.001	0.265	0.008	0.219	0.029
Ovarian size	0.063	0.534	0.362	<0.001	0.287	0.004
Hyperandrogenemia	0.257	0.010	0.375	<0.001	0.362	<0.001
HOMA-IR score	0.224	0.025	0.241	0.016	0.122	0.225
CIMT	0.412	<0.001	-	-	0.263	0.008
CRR	0.263	0.008	0.361	<0.001	-	-

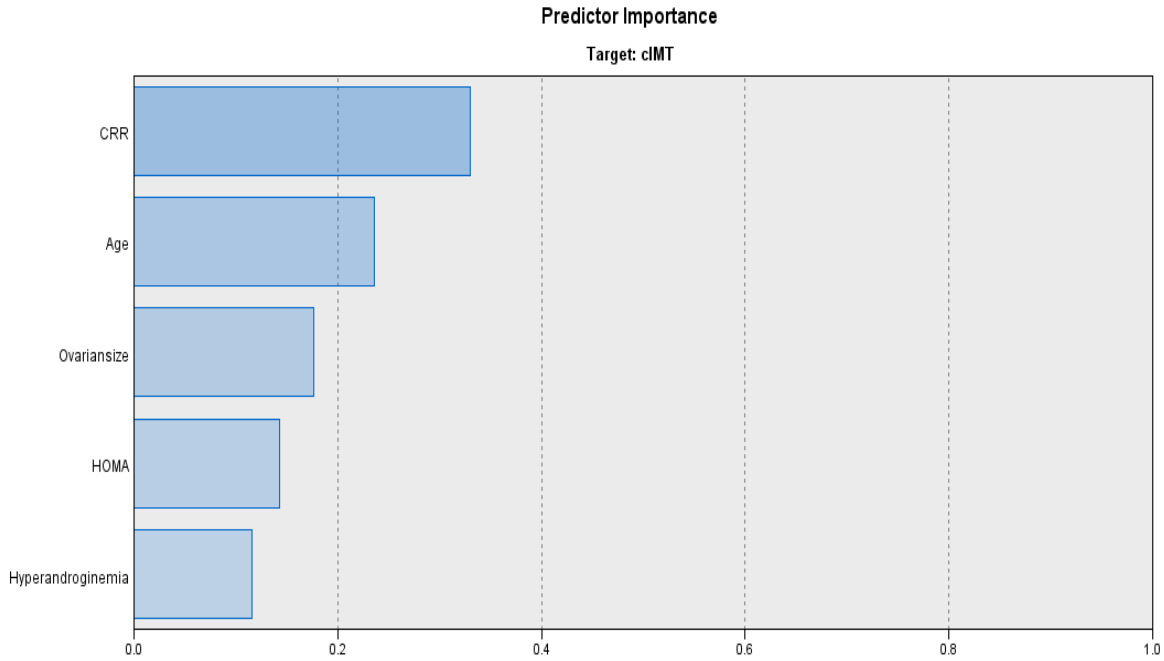

Fig. (2): Importance of variables correlated with cardiac risk markers as predictors for high CIMT

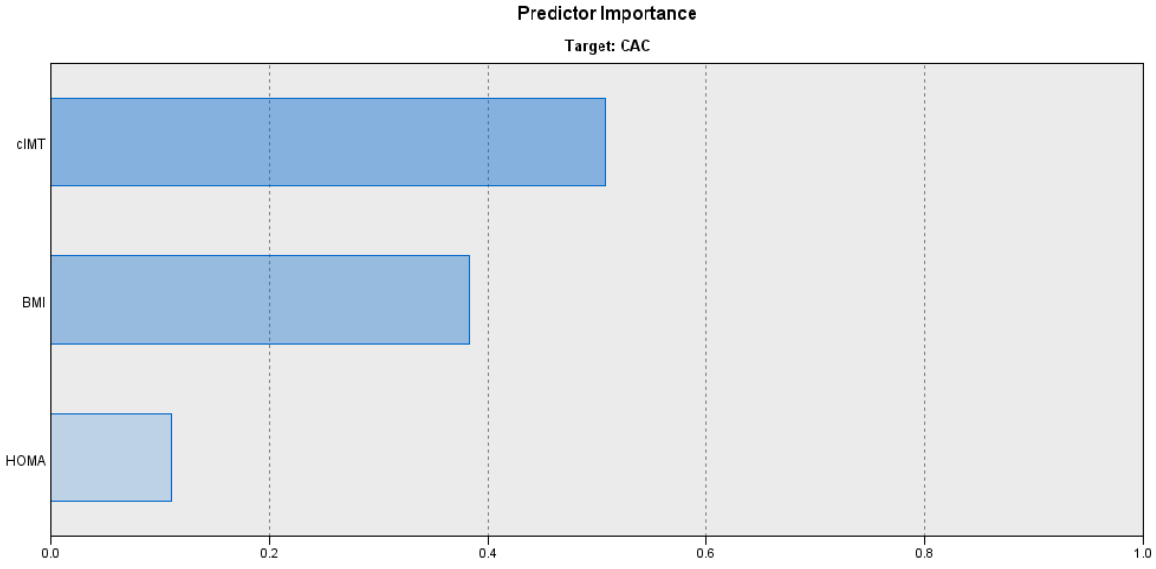

Fig. (3): Importance of variables correlated with cardiac risk markers as predictors for high CAC score

ROC curve analysis using multivariate analysis for BMI, CIMT and HOMA-IR as sensitive predictors for high CAC score as judged by the significance of the area under the curve (AUC) compared to the area under the reference line defined high BMI as the most significant predictor with AUC of 0.287 (±0.056; 95% CI: 0.177-0.397) and P-value <0.001, followed by high CIMT with AUC of 0.347 (±0.054; 95% CI: 0.241-0.454) and P-value of 0.011; while HOMA-IR score was non-significant predictor with AUC of 0.448 (±0.059; 95% CI: 0.333-0.563) and P-value of 0.128 as shown in figure 4.

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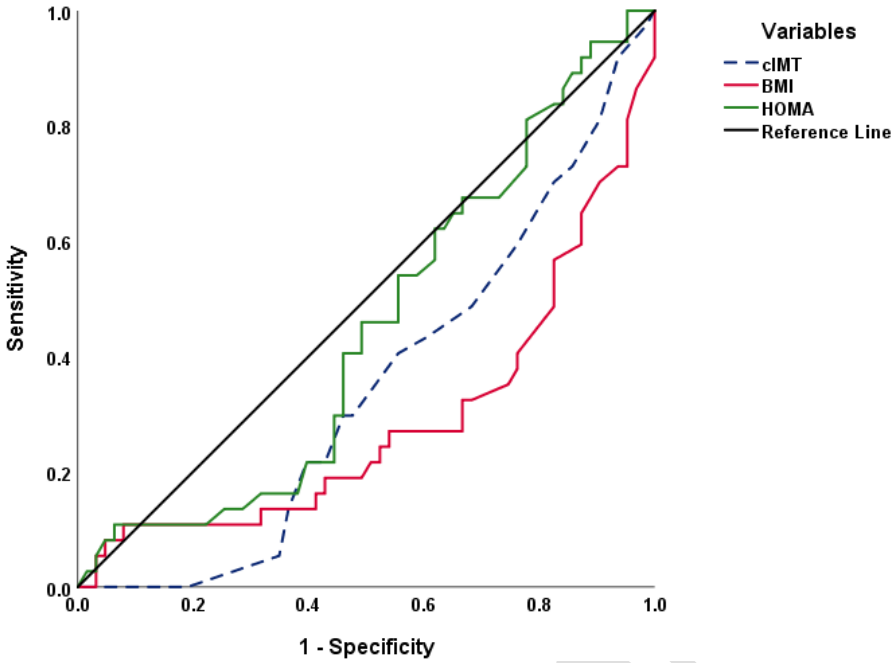

Fig. (4): ROC curve analysis of the most important predictors for high CAC score as determined by the Automatic Linear Modeling analysis

Discussion

The current study detected significant differences between cardiac asymptomatic adult PCOS women older than thirties and their age-matched control fertile women as regards cardiac risk ratio (CRR), the carotid intima-media thickness (CIMT) and the coronary artery calcification (CAC) score. These findings point to the fact that these women, despite being apparently healthy and cardiac asymptomatic are at risk of development of cardiovascular diseases (CVD) or cerebral insults.

Similarly, one study reported a Hazard ratio (HR) of 1.7 for CVD development in PCOS Denmark women with a total event rate of CVD of 22.6 versus 13.2/1000 women/year in controls and PCOS women were significantly younger at time of CVD diagnosis than controls (26). Another study also found the overall incidence of coronary artery disease (CAD) was 63% higher in PCOS women than in controls (27). Thereafter, a literature review found PCOS women had increased risks of hypertension and non-fatal cerebrovascular disease events compared to women without PCOS (28) and one comparative study reported that normotensive non-obese PCOS women were prone to have higher left ventricular mass index than

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healthy controls and it was positively correlated with insulin resistance (29).

Further, two recent studies documented that PCOS women are more likely to develop hypertension from early adulthood, independent of BMI (30, 31). Moreover, it was reported that the crude rates of the myocardial infarction, stroke, angina, revascularization, and cardiovascular mortality were higher in PCOS women than control women (32).

The detected significantly higher CRR and HOMA-IR score for POCS women goes in hand with a previous study that detected a prevalence of IR was 39.6 to 55%, glucose intolerance rate was 7.2-28.1% and that of dyslipidemia was 54.1- 70.4% among PCOS women in different Brazilian regions (33). Further, significant correlations were reported between CRR and HOMA-IR score and with CIMT and CAC score. Thus, the detected high cardiac risk as judged by the estimated CIMT and CAC could be attributed to the PCOS-associated metabolic disturbance in diabetogenic direction, and the detected positive correlation between cardiac risk markers and BMI may be the underlying mechanism for the reported high cardiac risk.

These findings are coincident with the previously detected increased incidence of CAD by 20-fold greater in PCOS women with cardiometabolic comorbidities than those free of these comorbidities (27). Further, it was found that the genetic risk of obesity and metabolic effects are the common denominator of both PCOS and CAD risk (34). Also, it was detected that PCOS-induced hypertension is aggravated by obesity (30) and PCOS-associated obesity and hyperandrogenemia may explain the association between PCOS and cardiometabolic diseases (35).

Statistical analyses defined high CRR and HOMA-IR score and severity of hyperandrogenemia as the important predictor of high CIMT, while high CIMT, BMI and HOMA-IR could predict CAC score. Thus, the severity of metabolic disturbances in association with obesity is the most important predictors for CV insults.

In line with these findings, the results of a previous study suggested that obesity not hyperandrogenemia negatively related to early development CV risk markers in PCOS women (36). Another study indicated increased CV risk and found the diagnostic features of PCOS are the strongest predictor of CIMT (37). Then, CV parameters in PCOS women were independently associated with BMI with significantly higher CIMT measures in women with BMI levels ≥25 kg/m^2 than in women had BMI levels <25 kg/m^2 (38).

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In support of the role of obesity as a coronary risk factor, one study detected significantly higher prevalence of CAC in obese than in non-obese (39) and CAC score of 1-99 AU can predict high-risk plaque (40). Moreover, it was found that bariatric surgery for severe obesity significantly reduces the future risk of developing CV comorbidities with significant reduction in CAC scores (41).

Conclusion

Adult cardiac asymptomatic PCOS women older than thirties had high cardiovascular risk. Estimation of coronary risk ratio is non-invasive, cheap and available screening tool and had predictive ability for detection of women had high CIMT. CIMT is a minimally invasive diagnostic modality that can predict the extent of coronary artery calcification.

Recommendation

PCOS women older than thirties must be considered as cardiac risky patients even if they were asymptomatic and so evaluation of atherosclerotic status of these women using estimation of CRR and CIMT must be a part of routine evaluation.

Limitations

No intervention was undertaken to reduce the predisposing factors for such high cardiac risk.

References

1. Cunha A, & Póvoa AM: Infertility management in women with polycystic ovary syndrome: a review. Porto Biomed J. 2021 Jan 26; 6(1):e116. Doi: 10.1097/j.pbj.0000000000000116.
2. Sarahian N, Sarvazad H, Sajadi E, Rahnejat N, & Roozbahani N: Investigation of common risk factors between polycystic ovary syndrome and Alzheimer's disease: a narrative review. Reprod Health. 2021 Jul 26; 18(1):156. Doi: 10.1186/s12978-021-01203-x.
3. Dondi E, Tufano M, Vigone M, Lucaccioni L, Pozzobon G, Ubertini G, et al: Polycystic ovary syndrome in pediatric obesity and diabetes. Minerva Pediatr (Torino). 2021 Jul 21. Doi: 10.23736/S2724-5276.21.06542-3.
4. Cignarella A, Mioni R, Sabbadin C, Dassie F, Parolin M, Vettor R, et al: Pharmacological Approaches to Controlling Cardiometabolic Risk in Women with PCOS. Int J Mol Sci. 2020 Dec 15; 21(24):9554. Doi: 10.3390/ijms21249554.
5. Amadi C, Lawal F, Ajiboye W, Agbim R, Mbakwem A, Ajuluchukwu J, et al: Opportunistic screening of cardiovascular disease risk factors in community pharmacies in Nigeria: a cross-sectional study. Int J Clin Pharm. 2020 Dec; 42(6):1469-1479. Doi: 10.1007/s11096-020-01112-2.
6. Aparicio R, Ball J, Yiallourou S, Venkataraman P, Marwick T, & Carrington M: Imaging-guided evaluation of subclinical atherosclerosis to enhance cardiovascular risk prediction in asymptomatic low-to-intermediate risk individuals: A systematic review. Prev Med. 2021 Dec; 153:106819. Doi: 10.1016/j.ypmed.2021.106819.
7. Chen L, Wang G, He J, Yang X, Zheng Z, Deng Y, et al: SIRT6 inhibits endothelial-to-mesenchymal transition through attenuating the vascular endothelial inflammatory response. Int Immunopharmacol. 2021 Oct 16; 101(Pt B):108240. Doi: 10.1016/j.intimp.2021.108240.
8. Poredos P, & Jezovnik MK: Preclinical carotid atherosclerosis as an indicator of polyvascular disease: a narrative review. Ann Transl Med. 2021 Jul; 9(14):1204. Doi: 10.21037/atm-20-5570.
9. Novo S, Diana D, Tomasino C, Zambelli G, Mignano A, Scalmato A, et al:

Electrocardiographic abnormalities, preclinical carotid atherosclerosis and cardiovascular risk in an apparently healthy real-world population. Data from the "No Stroke, No Infarction" project of the Rotary International - district 2110 (Sicily and Malta). Int Angiol. 2021 Dec; 40(6):470-477. Doi: 10.23736/S0392-9590.21.04637-X.

10. Cainzos-Achirica M, Anugula D, Mszar R, Grandhi G, Patel K, Bittencourt M, et al: Rationale and pathways forward in the implementation of coronary artery calcium-based enrichment of randomized trials. Am Heart J. 2022 Jan; 243:54-65. Doi: 10.1016/j.ahj.2021.09.006.
11. Cruz D, Tahir U, Hu J, Ngo D, Chen Z, Robbins J, et al: Metabolomic Analysis of Coronary Heart Disease in an African American Cohort from the Jackson Heart Study. JAMA Cardiol. 2021 Dec 1. Doi: 10.1001/jamacardio.2021.4925.
12. Playford D, Hamilton-Craig C, Dwivedi G, & Figtree G: Examining the Potential for Coronary Artery Calcium (CAC) Scoring for Individuals at Low Cardiovascular Risk. Heart Lung Circ. 2021 Dec; 30(12):1819-1828. Doi: 10.1016/j.hlc.2021.04.026.
13. Chen MJ, Yang WS, Yang JH, Hsiao CK, Yang YS, & Ho HN: Low sex hormone-binding globulin is associated with low high-density lipoprotein cholesterol and metabolic syndrome in women with PCOS. Hum Reprod 2006; 21:2266–71.
14. Chen MJ, Yang WS, Yang JH, Chen CL, Ho HN, & Yang YS: Relationship between androgen levels and blood pressure in young women with polycystic ovary syndrome. Hypertension 2007; 49:1442–7.
15. Bray GA: Pathophysiology of obesity. Am J Clin Nutr, 1992; 55: 488S-94S.
16. WHO: Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. WHO Technical Report Series 854. Geneva: World Health Organization, 1995.
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, & Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia.1985; 28:412–19.
18. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al: Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr, 2015 Mar; 16(3):233-70. Doi: 10.1093/ehjci/jev014.
19. Pignoli P, Tremoli E, Poli A, Oreste P, & Paoletti R: Intimal plus medial thickness of the arterial wall: A direct measurement with ultrasound imaging. Circulation, 1986 Dec; 74(6):1399-406. Doi: 10.1161/01.cir.74.6.1399.
20. Hwang S, Onuma O, Massaro J, Zhang X, Fu Y, Hoffmann U, et al**:** Maintenance of Ideal Cardiovascular Health and Coronary Artery Calcium Progression in Low-Risk Men and Women in the Framingham Heart Study. Circ Cardiovasc Imaging. 2018 Jan; 11(1):e006209. Doi: 10.1161/CIRCIMAGING.117.006209.
21. Neves PO, Andrade J, & Monçao H: Coronary Artery Calcium Score: Current Status; Radiol Bras. 2017 Doi: 10.1590/0100-3984.2015.0235.
22. Thomas I, Forbang N, & Criqui M: The evolving view of coronary artery calcium and cardiovascular disease risk. Clin Cardiol. 2018 Jan; 41(1):144-150. Doi: 10.1002/clc.22842.
23. Genest J, Frohlich J, & Fodor G, McPherson R: the Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: 2003 update. CMAJ. 2003; 169: 921–4.
24. Millán J, Pintó X, Muñoz A, Manuel Zúñiga M, Rubiés-Prat J, Felipe Pallardo L, et al: Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. Vasc Health Risk Manag, 2009; 5: 757–65.
25. Talbott EO, Zborowski J, Rager J, & Stragand JR.: Is there an independent effect of polycystic ovary syndrome (PCOS) and menopause on the prevalence of subclinical atherosclerosis in middle aged women? Vasc Health Risk Manag. 2008;4(2):453-62
26. Glintborg D, Rubin K, Nybo M, Abrahamsen B, & Andersen M: Cardiovascular disease in a nationwide population of Danish women with polycystic ovary syndrome. Cardiovasc Diabetol. 2018 Mar 8; 17(1):37. Doi: 10.1186/s12933-018-0680-5.
27. Ding D, Tsai I, Wang J, Lin S, & Sung F: Coronary artery disease risk in young women

with polycystic ovary syndrome. Oncotarget. 2018 Jan 4; 9(9):8756-8764. Doi: 10.18632/oncotarget.23985.

28. Wekker V, van Dammen L, Koning A, Heida K, Painter R, Limpens J, et al: Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. Hum Reprod Update. 2020 Nov 1; 26(6):942-960. Doi: 10.1093/humupd/dmaa029

29. Rashid A, Masood A, Wani I, Hafeez I, Parvez T, Zagar M, et al: Left ventricular myocardial mass index and its correlates as an early marker of cardiovascular risk among nonobese normotensive Indian women with polycystic ovary syndrome: lessons from a cross-sectional study. Fertil Steril. 2020 Jun; 113(6):1299-1307.e2. Doi: 10.1016/j.fertnstert.2020.02.001.

30. Joham A, Kakoly N, Teede H, & Earnest A: Incidence and Predictors of Hypertension in a Cohort of Australian Women with and Without Polycystic Ovary Syndrome. J Clin Endocrinol Metab. 2021 May 13; 106(6):1585-1593. Doi: 10.1210/clinem/dgab134.

31. Mellembakken JR, Mahmoudan A, Mørkrid L, Sundström-Poromaa I, Morin-Papunen L, Tapanainen J, et al: Higher blood pressure in normal weight women with PCOS compared to controls. Endocr Connect. 2021 Feb; 10(2):154-163. Doi: 10.1530/EC-20-0527.

32. Berni T, Morgan C, & Rees D: Women with Polycystic Ovary Syndrome Have an Increased Risk of Major Cardiovascular Events: a Population Study. J Clin Endocrinol Metab. 2021 Aug 18; 106(9): e3369-e3380. Doi: 10.1210/clinem/dgab392.

33. Maffazioli G, Lopes C, Heinrich-Oliveira V, Lobo R, Hayashida S, Soares Jr J, et al: Prevalence of metabolic disturbances among women with polycystic ovary syndrome in different regions of Brazil. Int J Gynaecol Obstet. 2020 Dec; 151(3):383-391. Doi: 10.1002/ijgo.13374.

34. Simons P, Cornelissen M, Valkenburg O, Onland-Moret N, van der Schouw Y, Stehouwer C, et al: Causal relationship between polycystic ovary syndrome and coronary artery disease: A Mendelian randomisation study. Clin Endocrinol (Oxf). 2021 Sep 15. Doi: 10.1111/cen.14593.

35. Zhu T, Cui J, & Goodarzi M: Polycystic Ovary Syndrome and Risk of Type 2 Diabetes, Coronary Heart Disease, and Stroke. Diabetes. 2021 Feb; 70(2):627-637. Doi: 10.2337/db20-0800.

36. Pandurevic S, Bergamaschi L, Pizzi C, Patton L, Rucci P, Corzani F, et al: Body mass index rather than the phenotype impacts precocious ultrasound cardiovascular risk markers in polycystic ovary syndrome. Eur J Endocrinol. 2021 Jan; 184(1):199-208. Doi: 10.1530/EJE-20-0725.

37. Jabbour R, Ott J, Eppel W, & Frigo P: Carotid intima-media thickness in polycystic ovary syndrome and its association with hormone and lipid profiles. PLoS One. 2020 Apr 24; 15(4):e0232299. Doi: 10.1371/journal.pone.0232299.

38. Tosun Ş, Gurbuz T, Cebi A, Tosun A, Gokmen O, & Usta M: Association of increased levels of omentin-1 and carotid intima-media thickness with early signs of cardiovascular risk in patients with polycystic ovary syndrome: A prospective case control study. J Obstet Gynaecol Res. 2021 Oct 22. Doi: 10.1111/jog.15077.

39. Lemanowicz A, Białecki M, Leszczyński W, & Hawrył M: Coronary age, based on coronary calcium measurement, is increased in patients with morbid obesity. Pol J Radiol. 2018 Sep 5; 83:e415-e420. Doi: 10.5114/pjr.2018.78624.

40. Senoner T, Plank F, Langer C, Beyer C, Steinkohl F, Barbieri F, et al: Smoking and obesity predict high-risk plaque by coronary CTA in low coronary artery calcium score (CACS). J Cardiovasc Comput Tomogr Nov-Dec 2021; 15(6):499-505. Doi: 10.1016/j.jcct.2021.04.003.

41. Salman A, Matter M, Fayad N, Shehata M, Abd Al-Fattah M, Elkaseer M, et al: Improvement of Coronary Calcium Scores After Bariatric Surgery in People with Severe Obesity. Obes Surg. 2021 Nov 22. Doi: 10.1007/s11695-021-05801-3.

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