Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

Association of second to fourth digit ratio (2D:4D) with risk prediction of coronary artery disease among females of North-West India

Dr Kanchan Dogra[1], Dr Nidhi Puri[2*], Dr Somya[3], Dr Deepak Puri[4]

[1](M.Sc Medical Anatomy), Department of Anatomy, Chirayu Medical College and Hospital, Bhopal (MP, India)-462030
[2]*(MS Anatomy), Department of Anatomy, AIIMS Bilaspur (HP, India)-174001
[3](MBBS) Junior Resident (Non-Academic) AIIMS Bilaspur (HP, India)-174001
[4](MCh CTVS), Department of CTVS, Max Superspeciality Hospital, Mohali (Punjab, India) - 160055

***Corresponding Author:** Dr Nidhi Puri
Email: drnidhipuri1@gmail.com

Abstract

Background: Coronary artery disease, a leading cause of morbidity and mortality in both the genders, needs noninvasive predicting factors to identify the risk at early stage. Second and fourth digit ratio (2D:4D) of hand has been associated with coronary artery disease among males but literature lacks such data in relation to female population.

Aim: To establish any association between 2D:4D ratio and coronary artery disease and with family history related to risk of coronary artery disease so as to assess the predictive value of digit ratio.

Material and Methods: The study was conducted on 200 adult female subjects of North India under two groups: 1. Control group- subjects with no known history of coronary artery disease, 2 Patient group- subjects with known history of coronary artery disease (CAD). Family history of CAD, hypertension (HT) and diabetes mellites (DM) was noted. The index finger (2D) and the ring finger (4D) lengths were measured to calculate 2D:4D ratio.

Results: Mean right and left 2D:4D ratio was significantly higher group 2. With medium effect size and Odd's ratio (1.83), Right 2D:4D ratio is a better risk predictor. The prevalence of high right 2D:4D ratio was significantly more among subjects having positive family history reflecting risk of CAD in both groups.

Conclusion: Association of high right 2D:4D ratio with coronary artery disease and relevant family history shows risk prediction for coronary artery disease among females.

Key words: CAD risk predictor, coronary artery disease, Digit ratio, 2D:4D ratio, 2D:4D in CAD

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Introduction

Coronary artery disease (CAD) has been a leading cause of mortality and loss of disability adjusted life years (DALYs) globally since last two decades.[1] It is the leading cause of death in men as well as in women, although presentation in women is, on average, 7-10 years later. Recent studies have reported declining trends of CAD in incidence and mortality among men but not among women.[2] It accounts for one out of three deaths of women regardless of race or ethnicity.[3] Burden of disease is more prevalent in low- and middle-income countries. India accounts for one fifth of cardiovascular disease (CVD) related mortality worldwide.[4] Indian population also has the highest prevalence of CAD and the conventional risk factors are not able to explain this increased risk. Moreover, early onset, rapid progression and high mortality rate has made CAD the cause of concern for Indian papulation. Coronary artery disease is on rise among women from urban as well as rural parts of India.[5] Since CAD has non modifiable as well as modifiable risk factors, modification in lifestyle at an earlier age can prove helpful in preventing an event at a later stage and slow down progression of disease. It is very important to identify the population at risk of developing CAD to inculcate healthy lifestyle modification among at risk population. Therefore, a noninvasive method to evaluate the risk of developing the said disease is the need of the hour. Digit ratio (Ratio of index finger to the ring finger) has shown correlation with many non-communicable diseases including CAD in men.[6-7] Another study on male cadavers has reported presence of atherosclerotic plaque in right coronary artery with mean 2D:4D ratio of right hand more than 0.985 ± 0.017.[8] However, there is no literature available of such correlation among females, therefore the study was designed to establish any association between 2D:4D ratio and coronary artery disease as well as with family history related to risk of coronary artery disease to assess the predictive value of digit ratio.

Material & Methods

The present study was a cross-sectional study conducted on 200 adult female subjects of North India among the age group of 18-80 years. The subjects were studied under two groups. Group1 comprised of subjects with no known history of coronary artery disease (CAD) and group 2 included known patient of CAD. Prior informed, written consent for the study was obtained from the subject in both English and Vernacular. Subjects with apparent anomalies, inflammation, trauma, surgeries (if any) of hand were excluded. A family history of coronary artery disease, hypertension and diabetes mellitus was noted. The index finger (2D) and the ring finger (4D) lengths were measured with Vernier caliper on the palmer

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

aspect of both the hands from the middle of the proximal crease to the middle of the tip of the digit. These measurements were used to calculate ratio between index and ring finger (2D:4D). Since digit ratio more than 0.985 has been shown to be associated with atherosclerotic plaque,[8] subjects having 2D:4D ratio more than 0.985 were noted. Percentage of study subjects having 2D:4D ratio more than 0.985 was observed in both the groups and a prevalence of high digit ratio in relation to presence or absence of relevant family history was calculated.

Comparison of mean value 2D:4D ratio among subject with or without any family history of CAD and/ or HT and/ or DM was done to find out any association between high 2D:4D ratio and family history predicting risk of coronary artery disease.

Microsoft office excel was used for data entry and the SPSS (statistical package for social science, version20), Epi Info version7 were used for data analysis. Mean, standard deviation, frequencies (number of cases), and relative frequencies (percentages) were used as required. Student t-test (p value), Chi-Square test (x^2), Cohen's effect size (d), Odds Ratio and Confidence Interval (C.I.) were used to investigate the relationship between 2D:4D ratio and coronary artery disease among study groups. The probability value less than or equal to 0.05 was considered to be statistically significant. Cohen's effect size was classified as small -0.1-0.3, Medium- > 0.3-0.5, large- >0.5.[9]

Results

In the present study, data regarding 2D:4D was collected from a sample of 200 adult female subjects (100 without evidence of CAD and 100 CAD patients) among the age 18-80 years of age. Mean value for Rt. 2D:4D and Lt. 2D:4D was significantly higher in the patient group (table 1). Cohen's effect size of difference was medium for right 2D:4D and it was small for left 2D:4D (Table 2). 2D: 4D ratio was significantly higher on right side in both the groups (Table 3). Rt. 2D:4D ratio is a better risk predictor than the Lt. 2D:4D (Table 4). Right 2D:4D was significantly higher among subjects having positive family history of CAD and/or DM and/or HT in patient as well as control group (p value 0.005 and 0.034 respectively). Prevalence of digit ratio > 0.985 was 42.47% in group 1 and 55.17% in group 2 among subjects with family history and this difference was significantly higher than subject without relevant family history in group 2 (p value = 0.031).

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Figure 1-**a**: 2D:4D ratio in control group with and without family history. 1-**b:** 2D:4D ratio in patient group with and without family history

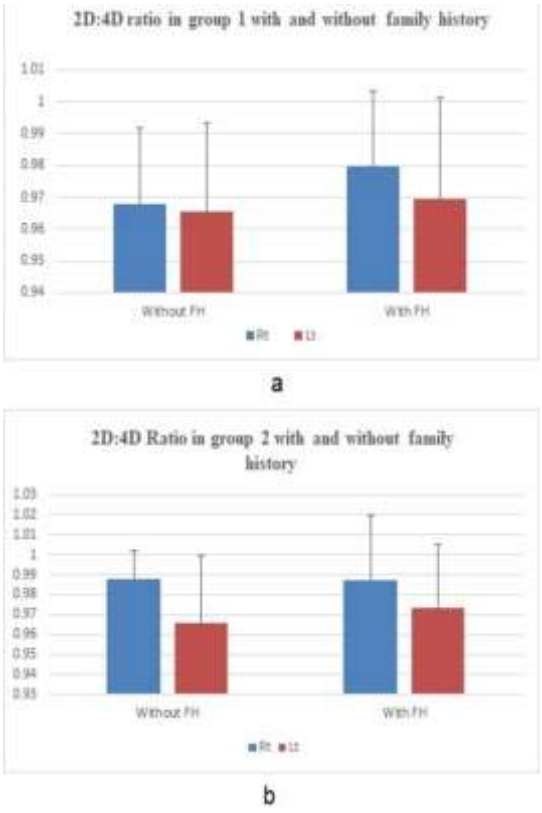

Figure 2: prevalence of digit ratio >0.985 in subjects with and without family history

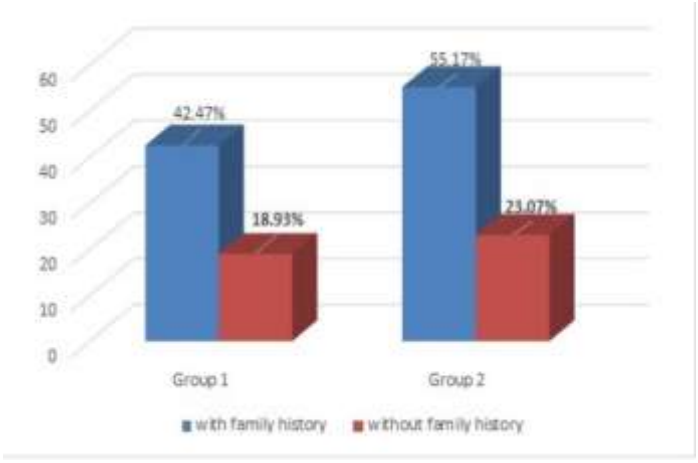

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Table 1. Comparison of various parameters among two groups

Variables	Control Group (n = 100)	Patient Group (n = 100)	p Value
	Mean ±SD	Mean ±SD	
AGE	31.21±8.61	62.64±9.16	0.00*
Rt. 2D	6.803±0.42	6.902±0.53	0.15
Rt. 4D Length	6.963±0.40	7.017±0.54	0.43
Lt. 2D Length	6.691±0.43	6.842±0.51	0.03*
Lt. 4D Length	6.910±0.39	7.046±0.49	0.03*
Rt. 2D:4D	0.977±0.03	0.987±0.03	0.01*
Lt. 2D:4D	0.968±0.02	0.973±0.032	0.32
*p value <0.05 have been considered statistically significant.			

Table 2: Cohen's effect size of Rt. & Lt. 2D:4D ratio among control and patient group

Digit Ratio	Control Group (Mean±SD)	Patient Group (Mean±SD)	Cohen's Effect Size
Rt. 2D:4D	0.977±0.03	0.987±0.03	0.35
Lt. 2D:4D	0.968±0.03	0.973±0.032	0.16
Cohen effect size: small -0.1-0.3, Medium- > 0.3-0.5, large- >0.5			

Table 3: difference of right and left 2D:4D ratio in both groups

Study Group	Rt 2D:4D	Lt 2D:4D	P value
Control group	0.977±0.027	0.96826±0.02982	0.031
Patient Group	0.9872 ± 0.03002	0.973±0.032	0.0022

Table 4: Odds Ratio, Confidence Interval, Chi-Square Values of digit ratio

Parameters	Odds ratio (O.R.)	Confidence interval (C.I.)	Chi square value ($x^{2)}$	P value
Rt. 2D:4D	1.83	95% [1.045-3.207]	4.50	0.03*
Lt.2D:4D	1.22	95% [0.701-2.130]	0.50	0.47

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Discussion

The 2D:4D is the most studied digit ratio and gender difference was first reported in literature in 1888.[9] The 2D:4D has been shown to be associated with many behavioral traits and many non-communicable diseases. [6,7,10] Its correlation has been seen with coronary artery disease in men but no such association is reported in literature among women.

In present study 2D:4D was high in the right hand among both the study groups and this difference with that of left hand was statistically significant. This ratio was higher among subjects having coronary artery disease and the difference was statistically significant (Table 1). Many previously published studies have shown right to left asymmetry not only in males but also in females. [11-13] The mean value of 2D:4D ratio in group 2 (Table 1) was similar to another study where mean 2D:4D ratio more than 0.985 ± 0.017 was corresponding with atherosclerotic plaque in right coronary artery. [8] Therefore, it was evident that high right 2D:4D is associated with coronary artery disease.

An experimental study on Rhesus monkey has revealed that increased right 2D:4D ratio in females is associated with early prenatal androgenic activity and excess of prenatal testosterone is reported to act as an endocrine disruptor to cause defective gonadal steroidogenesis, generating alterations in plasma testosterone thus controlling Protein Kinase C delta (PKCδ) enzyme expression via transcriptional regulation to cause enhanced vasoconstriction and hypertension in adult female. [14-15] Another prospective study on human subjects from Australia has also reported that high prenatal testosterone is associated with high blood pressure. [16] An association of raised prenatal testosterone levels with high right 2D:4D ratio and hypertension makes this digit ratio not only nonmodifiable factor but also a risk factor for hypertension. Since hypertension is one of the major risk factors of coronary artery disease therefore higher 2D:4D ratio can be associated with higher risk of developing CAD**.**

Effect size calculates magnitude of the experimental effect and size of association between two variables. [17] In the present study Cohen's effect size was found to be medium for right hand and small for the left hand (Table 2). This indicates that the difference of 2D:4D ratio

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for the right hand is high and is associated with a predisposition towards CAD in North Indian women. A study from China, among men has also reported a higher Cohan's effect size for right 2D:4D ratio. [6] As Odds ratio was more than one for right 2D:4D ratio therefore high right 2D:4D ratio was indicative of risk of developing CAD in future among all subjects (table 4). Moreover, the mean digit ratio of right hand was also found significantly higher among subjects of both the groups having family history of either CAD or diabetes mellites or hypertension (figure 1). Considering 2D:4D ratio more than 0.985 having associated with predisposition of atherosclerotic plaque in coronary artery,[8] prevalence of having 2D:4D more than 0.985 was found to be significantly higher among those with positive family history (figure 2). A study on Malaysian population has also reported that more than 60% of the study population with positive family history had digit ratio higher than one. [18] Therefore, association of high 2D:4D ratio with a positive family history is indicating its role as a predictor of CAD, however, a longitudinal study may elucidate enduring conclusion of high 2D:4D ratio as predictor of CAD among women.

Conclusion

Therefore, our findings suggest that high right 2D:4D ratio is a nonmodifiable risk factor. It is also found to be associated with coronary artery disease and family history predicting risk of CAD. This association indicates that high right 2D:4D ratio as predictor of CAD among the female population of north-west India.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

Financial Support and sponsorship: Nil

This article was previously presented as an oral paper at the 10th National Conference of Society of Clinical Anatomists (SOCA 2022) on May 27,2022

Conflict of interest: Nil

Statement by Authors: It is declared that:

- The manuscript has been read and approved by all the authors.
- The requirements for authorship have been met

Each author believes that the manuscript represents honest work and the contents were not published or sent previously to anywhere else for publications.

Suggestion: A longitudinal study is suggested to establish the role of 2D:4D ratio as predictor of CAD.

Acknowledgement: We thank the Department of Anatomy, MMIMSR, MM Deamed University Mullana (Haryana, India) for providing general support to conduct this study

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