Early Human Development 116 (2018) 64–67

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Digit ratio (2D:4D) and coronary artery disease in north Chinese women☆

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ARTICLE INFO

Keywords:
Digit ratio (2D:4D)
Sexual hormones
Coronary artery disease (CAD)

ABSTRACT

Background: Digit ratio (2D:4D) is fixed in utero and affected by fetal sex steroids. It has been proposed as a putative biomarker of certain hormone- related adult life traits and diseases. Several evidence suggest that 2D:4D ratio may correlate with cardiovascular disease risk (e.g., coronary artery disease).
Aims: To investigate whether there is a possible relationship between digit ratio (especially 2D:4D ratio) and coronary artery disease (CAD), and age at CAD in north Chinese women.
Methods: Photographs of the two hands of 303 females (controls: 194; patients: 109) were collected. Left hand, right hand and right minus left hand (Dr-l) digit ratio were analyzed and compared.
Results: The mean values of digit ratio in patients with CAD were lower than controls for each hand. Significant differences of 2D:4D (left and right hand: $P < 0.01$), 2D:5D (left hand: $P < 0.01$; right hand: $P < 0.05$) and 3D:4D (left hand: $P < 0.01$) were found between two groups. There were no associations between 2D:4D ratio and age at CAD on both hands.
Conclusion: Decreased digit ratio (especially 2D:4D ratio) may suggest a higher prenatal testosterone (lower prenatal oestrogen) exposure in north Chinese women with coronary artery disease.

1. Introduction

Cardiovascular disease is the most prevalent non-communicable cause of death worldwide and within this coronary artery disease (CAD) is one of the leading causes of death (World Health Statistics 2009, World Health Organization) [1]. When compared with women, men seem to have higher mortality and morbidity. These differences may be related, partly at least, to differences in prenatal levels and ratios of sex steroids in males and females [1]. Since it is not possible to directly measure the prenatal concentrations of testosterone/oestrogen in adults, a simple and reliable indicator for identifying the individuals at risk of disease in the early stages of life is necessary.

It has been commonly believed that digit ratio, especially the second to fourth digit ratio (2D:4D) is a marker of prenatal exposure to sex hormones [2]. Low 2D:4D ratio indicates high prenatal testosterone (PT) exposure, and high 2D:4D ratio indicates high prenatal oestrogen (PE) exposure. In recent years, a number of researchers have focus on the relationship between 2D:4D ratio with traits in numerous studies of disease in adulthood, such as cardiovascular disease, certain cancers and reproduction [3–9]. Moreover, several evidence suggested that the prenatal balance of sex hormones, reflected in the 2D:4D ratio, might have a multilateral long-term effect on the human biological condition and might affect adult disease risk, especially those sex steroids related diseases [4–6,8,10].

Up to date, measures adopted to investigate the correlation between 2D:4D and cardiovascular disease, including CAD has been discussed in several ethnic groups [3–5,11–13]. The first paper that reported a correlation on 2D:4D to age at presentation of first myocardial infarction (MI) in men was Manning and Bundred [12] who concluded that high 2D:4D (indicating low PT) may be a maker for risk of early MI in men, and this was followed up with a larger sample in Manning et al. [13]. The latter paper linked these findings to the association between low 2D:4D in men and endurance running speed that has been reported in a number of papers. In agreement with Manning and Bundred [12], after controlling for body mass index, Fink et al. [14] observed a significantly positive correlation between 2D:4D and neck circumference for men and suggested that the higher the 2D:4D ratio the higher the neck circumference indicated the higher risk of CAD. Subsequently, Kyriakidis et al. [15] also found that 2D:4D ratios were significantly higher in men with MI than in controls. Recently, similar results were confirmed in samples of Chinese men [5,7], in north Indian men [4]. In addition, a previous study by Manning et al. shown that 2D:3D and

☆ Foundation item: This study was supported by grants from National Natural Science Foundation of PR China (Grant No. 31460272; 30960154; 31360257)
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https://doi.org/10.1016/j.earlhumdev.2017.11.007
Received 5 October 2017; Received in revised form 19 November 2017; Accepted 21 November 2017
0378-3782/

2D:5D other than 2D:4D predict age at MI in men [16]. All the findings above in some way indicate that 2D:4D, including 2D:3D and 2D:5D (indicating PT/PE) may be useful indicators for predisposition MI and CAD in men. However, there is limit information for women. CAD is generally to be thought a hormonally driven disease [1]. Since the association between PT/PE and 2D:4D is at least as well substantiated in women as it is in men [17], if 2D:4D is associated with the risk of CAD in men, then we would hypothesize that there may be an possible association between them in women.

Given the above background, although Wu et al. have performed a study on the correlation between 2D:4D and CAD of Chinese men and women from an mixed regions (e.g., Beijin, Shangdong province) [3]. Here we conducted this work to investigate whether digit ratio (especially 2D:4D) is associated with CAD in north Chinese population (the Ningxia Hui Autonomous Region, North China) and in the meantime, to prove whether the findings of Wu et al. could be generalized to other groups of Chinese women.

2. Subjects and methods

2.1. Samples and study site

The study was performed at the Yinchuan city, which is located in the Ningxia Hui Autonomous Region of north China. The participants included 303 adult females (age: 30–69 years) in this city. The normal controls (n = 194, mean age ± S.D. = 56.37 ± 7.60 years) were exhibited healthy physical and mental states. All patients (n = 109, mean age ± S.D. = 55.50 ± 8.40 years) were diagnosed with coronary artery radiography confirmed CAD in the general hospital affiliated to Ningxia Medical University.

2.2. Ethical statements

The present study received approval from the Ethics Committee of Ningxia Medical University. All participants included in the study signed an informed consent.

2.3. Data collection

According to the report by Ribeiro et al. [18] which provides criticisms of the photocopy method, we choose the photographs method which is superior to that of photocopies as described by Frick et al. [19]. Briefly, participants were required to put their hands flat on a table and directly underneath a tripod mounted digital camera (DSCW520; Sony, Tokyo, Japan), with the palmar surface facing up and the fingers outstretched. All digit photographs were checked to insure the basal creases and the tips of each digit of both hands were clearly visible, and then input to the computer with the Image-Pro Plus 6.0 (Media Cybernetics, US) to measure the lengths of each digit (the basal creases and the tips at the midline) of both hands (accurate to 0.01 mm). To minimize measurement errors, each digit was measured twice and the average value was calculated as the last result. *Re*-measurement reliability of digit ratios (intraclass correlation coefficients, r_1) were: 2D:3D (left $r_1 = 0.94$, $F = 15.81$, $P < 0.001$; right $r_1 = 0.96$, $F = 26.25$, $P < 0.001$), 2D:4D (left $r_1 = 0.95$, $F = 21.99$, $P < 0.001$; right $r_1 = 0.98$, $F = 45.57$, $P < 0.001$), 2D:5D (left $r_1 = 0.97$, $F = 38.00$, $P < 0.001$; right $r_1 = 0.99$, $F = 55.94$, $P < 0.001$), 3D:4D (left $r_1 = 0.98$, $F = 51.33$, $P < 0.001$; right $r_1 = 0.97$, $F = 39.59$, $P < 0.001$), 3D:5D (left $r_1 = 0.97$, $F = 32.33$, $P < 0.001$; right $r_1 = 0.94$, $F = 34.20$, $P < 0.001$), 4D:5D(left $r_1 = 0.95$, $F = 37.93$, $P < 0.001$; right $r_1 = 0.91$, $F = 11.67$, $P < 0.001$). We concluded that our measurements of each digit ratio on both hands reflected real differences between individuals. Then each digit ratio for right and left hand were calculated by dividing the length of the corresponding digit and others respectively.

2.4. Statistical analysis

An independent sample *t*-test was performed to test the difference on digit ratio and age between controls and patients. The Pearson correlation coefficient test was used to explore the relationship between 2D:4D and age/age of onset. Data were all analyzed by SPSS software (v: 22.0), with a significance level of $P \le 0.05$.

3. Results

3.1. Mean values and range of digit ratio and age

The age range in controls (30–69 years) was similar to that in CAD patients (31–68 years). There was no significant difference between two groups on age ($t = -0.916$, $P = 0.360$).

In both groups, mean values of left and right hand digit ratio shown a similar trend as 2D:3D < 2D:4D < 3D:4D < 2D:5D < 4D:5D < 3D:5D. The CAD patients have lower mean values of all digit ratio than controls and significant differences of 2D:4D, 2D:5D on both hands and 3D:4D on left hand were found between two groups. There were no significant differences on other digit ratios (Table 1).

Given the relatively obvious differences in 2D:4D on both hands between two groups, we pay more attention to it later. The range of 2D:4D in two groups was also similar (Table 2). There were no significant differences between left hand and right hand in both groups (controls: $t = 0.271$, $P = 0.786$; patients: $t = 0.038$, $P = 0.970$). No significant difference was observed on Dr.-l ($t = -0.153$, $P = 0.878$) (Table 2).

3.2. Relationship between 2D:4D and age/age of onset

It has been shown: the 2D:4D ratio may be correlated with age at presentation of some hormone-related adult diseases [10–11]. Therefore, we test the relationship between 2D:4D and age/age of onset by using the simple linear regression analysis. No significant correlation between 2D:4D and age was observed in two groups respectively, and also no significant association was found between 2D:4D and the age of onset in patient group (all $P > 0.05$) (Table 3).

4. Discussion

Coronary artery disease (CAD) is an enormous health problem and rapidly increasing in prevalence across the world. Globally, although the chance of developing CAD is 2.2 times greater in men than in women [20], it is vital to maintain CAD patients of both sexes with a good quality of life. To the best of our knowledge, for the first time, the present study provides not only the information of digit ratio in CAD

Table 1
Mean values of digit ratio in controls and CAD patients (mean, SD).

Digit ratio	Hand	Controls(n = 194) Mean (SD)	CAD (n = 109) Mean (SD)	*t*	*P*
2D:3D	Left	0.895(0.024)	0.890(0.034)	− 1.002	0.368
	Right	0.889(0.027)	0.887(0.022)	− 0.992	0.322
2D:4D	Left	0.953(0.033)	0.940(0.033)	− 3.225	0.001**
	Right	0.952(0.034)	0.939(0.032)	− 3.015	0.003**
2D:5D	Left	1.208(0.066)	1.190(0.063)	− 2.876	0.004**
	Right	1.203(0.072)	1.187(0.055)	− 1.949	0.047*
3D:4D	Left	1.078(0.053)	1.069(0.062)	− 2.681	0.008**
	Right	1.072(0.043)	1.067(0.062)	− 1.950	0.052
3D:5D	Left	1.350(0.061)	1.340(0.063)	− 0.783	0.433
	Right	1.354(0.065)	1.347(0.050)	− 0.909	0.364
4D:5D	Left	1.265(0.043)	1.260(0.044)	− 0.748	0.472
	Right	1.262(0.053)	1.259(0.052)	− 0.703	0.482

* $P < 0.05$ (difference of digit ratio between CAD patients and controls).
** $P < 0.01$ (difference of digit ratio between CAD patients and controls).