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Digit (2D:4D) ratio is associated with muscle mass (MM) and strength (MS) in older adults: Possible effect of in utero androgen exposure

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ABSTRACT

Decline in MM and MS with aging, defined as sarcopenia, is related with physical disability, poor quality of life and death. Its mechanisms are not fully understood. Testosterone increases muscle protein synthesis. However, the effects of in utero androgen exposure to MM and MS in older adults have not been studied. In utero androgen exposure is inversely related with 2D:4D ratio. The aim of this study was to investigate the relationship between 2D:4D ratio as an indicator of in utero androgen exposure and MM and MS in elderly patients. A total of 151 older adults were included. Calf-circumference (CC) and skeletal muscle mass index (SMI) were used for the assessment of MM and hand grip strength for the assessment of MS. Mean age ± SD of the patients was 73.72 ± 6.23. Fifty-two (34.4%) of patients were male, 99 (65.6%) were female. Right and left 2D:4D were significantly and negatively correlated with hand grip strength ($r = -0.365$, $p = 0.018$ and $r = -0.434$, $p = 0.005$, respectively), CC ($r = -0.422$, $p = 0.002$ and $r = -0.459$, $p = 0.001$, respectively) and SMI ($r = -0.354$, $p = 0.018$ and $r = -0.348$, $p = 0.022$, respectively) in men. In women, right and left 2D:4D were significantly and negatively correlated with hand grip strength ($r = -0.252$, $p = 0.022$ and $r = -0.234$, $p = 0.033$, respectively), CC ($r = -0.229$, $p = 0.024$ and $r = -0.302$, $p = 0.003$, respectively) and SMI ($r = -0.382$, $p < 0.001$ and $r = -0.431$, $p < 0.001$, respectively). In this study, we found that 2D:4D ratio was significantly and negatively correlated with parameters depicting MM and MS which may suggest the possible role of in utero androgen exposure in the development of MM and MS loss in the elderly.

1. Introduction

Decline in MM and MS with aging, advanced form defined as sarcopenia, increase the risk of adverse outcomes such as physical disability, poor quality of life and death (Cruz-Jentoft et al., 2010). The mechanisms of loss of MM and MS are multifactorial, but still poorly understood (Bastiaanse, Hilgenkamp, Echteld, & Evenhuis, 2012; Muscaritoli et al., 2010). Some internal factors are inflammation, reductions of anabolic hormones, accumulation of free radicals and increases of apoptotic activities (Hamer & Molloy, 2009; Muscaritoli et al., 2010). External factors are disuse (including immobility and physical inactivity), protein and energy deficiency (Ferrando, Lane, Stuart, Davis-Street, & Wolfe, 1996; Muscaritoli et al., 2010; Paddon-Jones, 2006).

Testosterone increases muscle protein synthesis, and its effects on muscle are modulated by several factors including genetic background, nutrition, and exercise (Sakuma & Yamaguchi, 2012). In older adults, levels of testosterone decrease year to year and these patients become tend to loss of MM and MS (Feldman et al., 2002; Morley & Perry, 2003). However, we do not know the effects of in utero androgen exposure to MM and MS in older adults.

The ratio of the lengths of the index (2D) and ring (4D) fingers as measured by the 2D:4D ratio has been suggested as an indicator of prenatal androgen exposure, and low 2D:4D ratio reflecting higher in utero testosterone exposure (Fink, Manning, & Neave, 2006; Manning & Bundred, 2000; Rahman et al., 2011) and 2D:4D digit ratio does not change with aging (McIntyre, Ellison, Lieberman, Demerath, & Towne, 2005; van Anders, 2007).

The aim of this study was to investigate the relationship between 2D:4D ratio and MM and MS in elderly patients.

2. Materials and methods

A total of 151 older adults (aged 65 years or more) who were referred to the outpatient clinic of Geriatric Medicine at Hacettepe University Hospital for comprehensive geriatric assessment were included in this cross-sectional study.

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2.1. Measurement of 2D:4D ratio

Participants were asked to take off any jewelry or rings that would interfere with finger length measurements. Each patient's right and left hand were scanned in gray-scale using a Hewlett Packard scanner (Hewlett-Packard Company, Greeley, CO, USA) at 100 dpi to ensure that measurements were calibrated to a pixel per inch platform and stored in a custom-designed database until processing. Participants placed their hands gently on the surface of the scanner with the second to fifth fingers held parallel and the tip of the middle finger aligned with the wrist and elbow. Scanned hand images were analyzed using GIMP software (GNU Image Manipulation Program, version 2.6.4). The lengths of 2D and 4D of each hand were then measured using mouse controlled calipers. In each instance, calipers were positioned midline along the finger's basal crease and expanded to the edge of the finger tip. 2D:4D ratios for the left and right hands were obtained by dividing the measurement of 2D by 4D.

2.2. Measurement of MM

CC and SMI were used to measure MM. CC which has been considered to be the most sensitive anthropometric measure of MM in the elderly by the World Health Organization (1995), was measured using a standard anthropometric tape with the participant in standing position. The tape was wrapped around the calf of the non-dominant leg at the widest part to obtain the maximal circumference. Subcutaneous tissues were not compressed (Bastiaanse et al., 2012; Rolland et al., 2003).

Basal metabolic rate (BMR), fat mass (FM), free-fat mass (FFM), resistance and total body water (TBW) were measured by bioimpedance analysis (BIA). Skeletal muscle mass (SM) was calculated using the BIA parameters according to previous studies (Janssen, Heymsfield, Baumgartner, & Ross, 2000). SM (kg) = [0.401 $\times$ (height^2/resistance) + (3.825 $\times$ gender) − (0.071 $\times$ - age) + 5.102], where height is in cm; resistance is in ohms; for sex, men = 1 and women = 0; and age is in years. SMI was calculated by dividing absolute SM by height by meters squared (kg/m^2) (Chien, Huang, & Wu, 2008; Morishita et al., 2012).

2.3. Measurements of MS

Hand grip strength (Mathiowetz et al., 1985) was performed with the Takei TKK 5401 Digital Handgrip Dynamometer. Three measurements of maximum strength were taken in the dominant hand, in three repetitions with a hand dynamometer, and the highest value was recorded as maximal grip strength.

The patient's height was measured barefoot to the nearest 0.5 cm using a stadiometer. The body weight was ascertained in light clothing using BIA device (TBF-300, Tanita, Body Composition Analyzer). Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2). All patients were questioned for history of hypertension (HT), diabetes mellitus (DM), coronary heart disease (CHD), hyperlipidemia (HL), dementia and smoking. Mini-Nutritional Assessment-Short form (MNA-SF) is performed to determine nutritional status of elderly subjects (Cohendy, Rubenstein, & Eledjam, 2001).

Bloods were obtained from antecubital vein from all subjects between 8.30 and 10.00 am, after fasting for at least 8 h. Laboratory tests were evaluated, which consisted of complete blood count, vitamin B12, folate, creatinine, calcium (Ca), albumin, fasting plasma glucose (FPG), plasma levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), erythrocyte sedimentation rate (ESR) and thyroid stimulating hormone (TSH) by a hospital autoanalyzer.

Participants with injured fingers that may cause incorrect measurements of 2D:4D ratio and participants with severe edema, pace-maker, prosthesis and severe electrolyte imbalance that may result in incorrect measurements of BIA were excluded from the study. Informed consent has been obtained and procedures followed were in accordance with the institutional ethical standards of the responsible committee on human experimentation.

2.4. Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows 18.0 program was used for statistical analysis. All data were entered into a database and were verified by a second independent person. The variables were investigated using visual (histograms, probability plots) and analytical methods to determine whether or not they are normally distributed. Data are presented as mean and $\pm$SD for normally distributed variables. Categorical variables are shown as frequencies.

Correlation analysis between 2D:4D ratio and CC, hand grip strength and SMI were performed with Pearson test. Two-sided values of $p < 0.05$ were considered as statistically significant.

3. Results

A total of 151 older adults were evaluated in this study. Mean age $\pm$ SD of the patients was 73.72 $\pm$ 6.23. Fifty-two (34.4%) of patients were male, 99 (65.6%) were female. Demographic properties, laboratory and BIA parameters of study population are presented in Table 1.

Table 1
Demographic properties, laboratory and BIA parameters of study population.

Parameters	Male (n = 52)	Female (n = 99)	p
Age (years)	75.00 ± 6.39	73.06 ± 6.07	0.069
BMI (kg/m^2)	26.09 ± 5.66	30.33 ± 7.14	<0.001
MMSE (score)	26.68 ± 4.57	26.22 ± 5.02	0.602
MNA-SF	12.79 ± 2.22	12.41 ± 2.13	0.328
Right 2D:4D	0.94 ± 0.29	0.95 ± 0.29	0.002
Left 2D:4D	0.94 ± 0.28	0.96 ± 0.28	0.002
CC	37.05 ± 4.19	37.10 ± 3.78	0.944
SMI	10.96 ± 4.30	9.95 ± 3.34	0.146
HT	31 (59.6%)	83 (83.8%)	0.001
DM	14 (26.9%)	34 (34.3%)	0.462
CHD	11 (21.2%)	27 (27.3%)	0.438
HL	24 (46.2%)	69 (74.2%)	0.008
Dementia	8 (15.4%)	12 (12.1%)	0.617
Smoking	5 (9.8%)	3 (3.0%)	0.122
WBC (/μl)	6997.40 ± 2180.56	6968.00 ± 1671.15	0.937
HGB (g/dl)	14.11 ± 1.31	13.04 ± 1.15	<0.001
B12 vitamin (pg/ml)	373.08 ± 198.71	420.02 ± 218.13	0.500
Folat (ng/ml)	8.15 ± 4.32	9.13 ± 2.75	0.266
Creatinine (mg/dl)	1.03 ± 0.26	0.79 ± 0.18	<0.001
Ca (mg/dl)	9.14 ± 0.38	9.37 ± 0.36	0.003
Albumin (g/dl)	4.27 ± 0.34	4.24 ± 0.30	0.686
FPG (mg/dl)	93.62 ± 17.58	100.00 ± 49.00	0.445
TC (mg/dl)	172.75 ± 36.93	194.91 ± 43.38	0.040
TG (mg/dl)	113.07 ± 61.02	134.79 ± 57.73	0.067
LDL (mg/dl)	111.57 ± 37.32	127.77 ± 40.22	0.042
HDL (mg/dl)	52.43 ± 14.12	54.36 ± 12.66	0.506
ALT (U/l)	17.44 ± 9.54	19.23 ± 11.84	0.420
AST (U/l)	20.07 ± 4.88	23.22 ± 8.39	0.054
ESR (mm/h)	14.78 ± 9.54	23.74 ± 13.51	<0.001
TSH (Uıu/ml)	2.48 ± 2.33	2.01 ± 1.34	0.183
BMR (kcal)	1398.62 ± 287.24	1285.66 ± 139.83	0.016
FM (kg)	15.85 ± 11.27	25.39 ± 11.41	<0.001
FFM (kg)	56.29 ± 10.26	45.91 ± 7.33	<0.001
TBW (kg)	41.65 ± 8.75	33.61±.5.36	<0.001
Impedance (Ω)	405.71 ± 119.46	441.21 ± 127.78	0.127

MMSE: mini-mental state examination; WBC: white blood cell; HGB: hemoglobin.