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ORIGINAL ARTICLE

Second to fourth digit ratio: a predictor of adult penile length

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The second to fourth digit ratio (2D:4D) has been proposed as a putative biomarker for prenatal testosterone and covaries with the sensitivity of the androgen receptor (AR). Both prenatal testosterone and the AR play a central role in penile growth. In this study, we investigated the relationship between digit ratio and penile length. Korean men who were hospitalized for urological surgery at a single tertiary academic centre were examined in this study, and 144 men aged 20 years or older who gave informed consent were prospectively enrolled. Right-hand second- and fourth-digit lengths were measured by a single investigator prior to measurement of penile length. Under anaesthesia, flaccid and stretched penile lengths were measured by another investigator who did not measure nor have any the information regarding the digit lengths. Univariate and multivariate analysis using linear regression models showed that only height was a significant predictive factor for flaccid penile length (univariate analysis: r=0.185, P=0.026; multivariate analysis: r=0.172, P=0.038) and that only digit ratio was a significant predictive factor for stretched penile length (univariate analysis: r=−0.216, P=0.009; multivariate analysis: r=−0.201, P=0.024; stretched penile length=−9.201×digit ratio + 20.577). Based on this evidence, we suggest that the digit ratio can predict adult penile size and that the effects of prenatal testosterone may in part explain the differences in adult penile length.

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INTRODUCTION

The ratio of second to fourth digit length (digit ratio, 2D:4D) is sexually dimorphic in humans (the mean digit ratio is lower in males than females)[1–5] and is thought to be fixed early in development.[6–10] Across vertebrate species including humans, the *Homeobox* (*Hox*) *a* and *d* genes regulate limb development, including fingers and toes, as well as development of the urogenital system, including testes, ovaries and penises.[6,7,11,12] Manning *et al.*[13] observed that the mean testis volume was significantly negatively correlated with the right digit ratio in azoospermic men.[13] These observations have led to the suggestion that patterns of digit formation may be related to gonad function.[1,11,14]

A previous study reported that the digit ratio of the right hand was negatively correlated with the foetal testosterone/foetal estradiol ratio.[15] As a result, a high level of foetal testosterone relative to foetal estradiol is associated with a low digit ratio. More convincing evidence regarding a link between prenatal testosterone and digit ratio comes from observations of digit ratios in girls with congenital adrenal hyperplasia[4] and in genetic males with complete androgen insensitivity.[16]

A lack of association between digit ratio and circulating testosterone levels[17] and the longitudinal stability of digit ratio[18] has also been reported. These findings add to the evidence demonstrating that digit ratio is a suitable tool to study the effects of prenatal androgen. Furthermore, it has recently been suggested that the digit ratio of the right hand is related to the activity of the androgen receptor (AR).[19]

Like digit development, penile growth is influenced by prenatal testosterone.[20–26] Androgens and a functioning androgen receptor are known to be necessary for normal development of the human penis.[20,26–31] However, to date, there have been few studies that reveal why men who undergo normal puberty have different penile lengths.

Based on these evidences, we hypothesized that prenatal testosterone levels play a possible role in different penile lengths and considered the possibility that digit ratio might be related to penile length; therefore, we investigated the relationship between digit ratio and penile length.

MATERIALS AND METHODS

Korean men hospitalized for urological surgery at a single tertiary academic centre were examined in this study, and 144 men aged 20 years or older were prospectively enrolled. Institutional Review Board approvals were obtained and all patients gave informed consent. Men with hypospadia, urethral stricture, Peyronie's disease, penile cancer, or a history of endocrine disease, urethroplasty or other penile surgery (except for circumcision) that has a major influence on penile length were excluded.

All the patients' height, weight, and finger and penile lengths were measured. The second and fourth digit lengths of the right hand were measured by a single investigator prior to measurement of penile length. Using a digital Vernier calliper accurate to 0.01 mm, digit lengths were measured directly on the ventral surfaces of the fingers, from the crease proximal to the palm at the base of each digit to the digit tip.[1] To minimize measurement errors, mean values of two digit ratios that were calculated from duplicate measurements were used in

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the analysis. The intraclass correlation coefficient (ICC) of two repeated measures of digit ratio by a single investigator was 0.967, which was similar to that of the study by Allaway *et al.*[32] (ICC_1=0.873, ICC_2=0.934, ICC_3=0.969). This suggests that a direct measurement of digit ratio using a digital Vernier calliper has acceptable repeatability.[33,34]

Penile lengths were measured by another single investigator who did not perform measurements or have any information regarding the digit lengths. Flaccid and fully stretched penile lengths were measured under anaesthesia. A rigid ruler was used to avoid measurement error due to penile curvature as described by Son *et al.*[35] In order to minimize the effect of temperature and touch on penile size, penile length measurements were taken immediately after the patient undressed. Measurements were taken, while patients were lying down and the legs were slightly abducted. The starting point was on the dorsal aspect of the penis at its base at the pubic-penile skin junction, pushing the prepubic fat pad against the pubic bone, as described by Wessells *et al.*,[36] and the tip of the penis was the other reference point. In order to reduce errors in measurement, two measurements were performed and their mean values were recorded.

Relationships between study variables were analysed using Pearson's linear correlation. To identify the independent predictive factors influencing penile length, univariate and multivariate analyses were performed using linear regression modelling. Analysis was performed using SPSS 12.0 (SPSS Inc., Chicago, IL, USA), and differences were considered statistically significant when P values were less than 0.05.

RESULTS

Patients' characteristics are summarized in **Table 1**. **Table 2** describes the detailed types of urology patients who were included in the study. None of the patients who were included in the study have a disease that has a strong influence on penile length (**Table 2**).

Table 3 summarizes the relationships between penile length and other study variables. Flaccid penile length was correlated with stretched penile length (r=0.727, P=0.000) (**Table 3**). In the univariate analysis using a linear regression model, height, body mass index (BMI) and digit ratio were associated with flaccid penile length. Among these three variables (height, BMI and digit ratio), only height was a significant predictive factor for flaccid penile length (r=0.172, P=0.038) in the multivariate analysis using a linear regression model. Similarly, in the univariate analysis using a linear regression model, height, the fourth-digit length and digit ratio were associated with stretched penile length. Among these three variables (height, fourth-digit length and digit ratio), only digit ratio was a significant predictive factor for stretched penile length (r=−0.201, P=0.024) in the multivariate analysis using a linear regression model (**Table 3**).

As shown in **Figure 1**, stretched penile length was found to be negatively associated with digit ratio. Penile ratio (stretched penile length/flaccid penile length) was negatively correlated with flaccid penile length (r=−0.698, P=0.000); however, it was not correlated with stretched penile length (r=−0.046, P=0.585) (**Table 3**).

Table 1 Characteristics of the study population (n=144)

	Mean±s.d.	*Median (range)*
Age (years)	57.3±16.5	59.0 (21.0–89.0)
Height (cm)	168.1±6.7	168.0 (152.0–184.0)
Weight (kg)	67.1±10.3	67.0 (45.0–100.0)
BMI (kg m^{-2})	23.72±3.08	23.53 (15.19–33.41)
Second-digit length (cm)	7.3±0.5	7.2 (6.2–8.6)
Fourth-digit length (cm)	7.5±0.6	7.4 (6.2–9.1)
Digit ratio	0.97±0.04	0.97 (0.88–1.12)
Flaccid penile length (cm)	7.7±1.7	7.8 (4.0–12.0)
Stretched penile length (cm)	11.7±1.9	11.5 (7.5–17.0)
Penile ratio	1.54±0.25	1.50 (1.15–2.44)

Abbreviations: BMI, body mass index; digit ratio, second digit length/fourth digit length; penile ratio, stretched penile length/flaccid penile length.

Table 2 Types of urology patients included in the study (n=144)

Site	*Diagnosis*	*Operation name*	*No.*
Kidney			21
	Renal cell carcinoma	Radical nephrectomy	15
	Renal cell carcinoma	Partial nephrectomy	1
	Non-function kidney	LESS nephrectomy (retroperitoneum)	1
	Renal stone	Percutaneous nephrolithotomy	4
Ureter			15
	Transitional cell carcinoma	Nephroureterectomy	5
	UPJ stricture	Acucise	2
	Upper ureter stone	Lapa ureterolithotomy	4
	Mid to lower ureter stone	Ureteroscopic stone removal	4
Bladder			45
	Bladder tumour	TURB	39
	Bladder tumour	Radical cystectomy	1
	Bladder stone	Cystolitholapaxy	3
	Bladder neck stricture	Transurethral incision	1
	Hematuria	Transurethral coagulation	1
Prostate			25
	Prostate cancer	Radical retropubic prostatectomy	12
	Benign prostate hyperplasia	TURP	11
	Benign prostate hyperplasia	Open prostatectomy	1
	R/O prostate cancer	Prostate biopsy (transperineal)	1
Scrotum			38
	Varicocele	Varicocelectomy	13
	S/P vasectomy	Vaso-vasostomy	4
	Male infertility	Epi-vasostomy	1
	Hydrocele	Hydrocelectomy	6
	Testicular tumour	Radical orchiectomy	4
	Undescended testis	Orchiopexy	2
	Epididymal cyst	Epididymal cyst excision	3
	Epididymitis	Epididymectomy	2
	Inguinal hernia	Herniorrhaphy	1
	Laceration	Wound repair	1
	Condyloma	Condyloma excision	1

Abbreviations: LESS, laparoendoscopic single-site; TURB, transurethral resection of bladder tumour; TURP, transurethral resection of prostate; UPJ, ureteropelvic junction.

DISCUSSION

Androgens and a functioning AR are known to be necessary for normal development of the human penis.[20,26–31] Although several studies have demonstrated that postnatal androgen exposure is important for penis growth,[23,25,37–39] penis formation and its capacity to grow are determined foetally by foetal androgen action.[20–26] Foetal androgen levels in males are elevated between weeks 8 and 24 of gestation, with peak levels occurring between weeks 14 and 16.[31] Activation of AR by prenatal testosterone also appears to contribute to the development of male internal genital structures and the differentiation of male external genitalia.[31]

Table 3 Relationships between penile length and other study variables

Variables	*Flaccid penile length*				*Stretched penile length*			
	Univariate		*Multivariate*		*Univariate*		*Multivariate*	
	r	P *value*	r	P *value*	r	P *value*	r	P *value*
Age	0.066	0.430			0.051	0.542		
Height	0.185	0.026	0.172	0.038	0.142	0.088	0.117	0.192
Weight	−0.035	0.677			0.016	0.845		
BMI	−0.147	0.079	−0.138	0.095	−0.064	0.449		
Second digit length	−0.036	0.664			0.001	0.989		
Fourth digit length	0.054	0.523			0.123	0.141	0.003	0.977
Digit ratio	−0.155	0.064	−0.122	0.141	−0.216	0.009	−0.201	0.024
Stretched penile length	0.727	0.000						
Penile ratio	−0.698	0.000			−0.046	0.585		

Abbreviations: BMI, body mass index; digit ratio, second digit length/fourth digit length; penile ratio, stretched penile length/flaccid penile length.

Several studies observed that *Homeobox* genes (*Hox a* and *d*) control the development of digits as well as the differentiation of testes and ovaries.[6,7,11,12] This observation has led to the suggestion that patterns of digit formation may be related to the development of the penis and to gonad function.[1,11,14]

Recently, Lutchmaya *et al.*[15] showed that the digit ratio of the right hand was negatively correlated with foetal testosterone/foetal estradiol ratio.[15] This may mean that digit ratio is sensitive to the effects of relative foetal testosterone and foetal oestrogen concentrations and that a high concentration of testosterone leads to a low digit ratio and suggests high prenatal testicular activity.[40]

Furthermore, Manning *et al.*[19] demonstrated that the digit ratio of the right hand is positively correlated with the number of CAG repeats in the *AR* gene and suggested that the digit ratio of the right hand is related to the activity of AR. It has been well established that the length of the CAG repeats is negatively related to sensitivity to testosterone.[41,42]

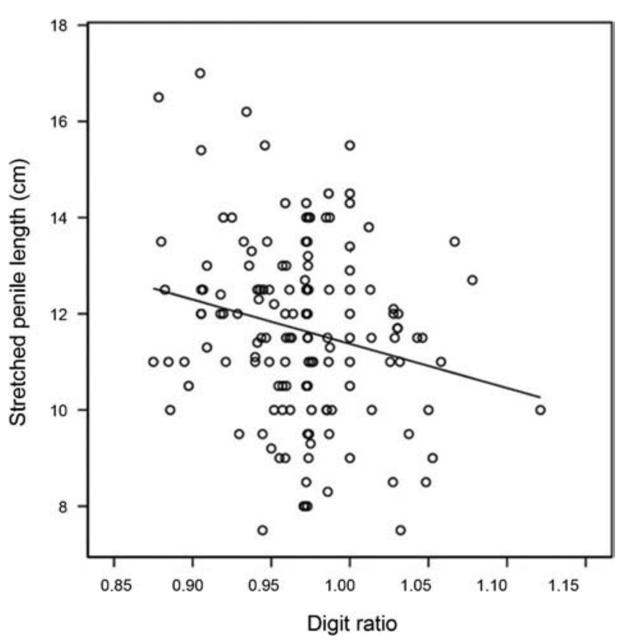

Figure 1 The relationship between digit ratio and stretched penile length. Stretched penile length was found to be negatively associated with digit ratio. $y=-9.201x+20.577$ ($r=-0.216$, $P=0.009$) (y: stretched penile length; x: digit ratio).

However, replication of this relationship between this *AR* gene polymorphism and digit ratio was largely unsuccessful.[43] Furthermore, although it seems that digit ratio is related to *Hox a* and *d* genes[6,7,11,12] and *AR* gene[19] polymorphism, a recent study[44] showed that digit ratio was not related to single-nucleotide polymorphisms in the *AR* gene or in the Hox cluster of genes but was instead related to variation in the *LIN28B* gene,[44] which has previously been associated with height[45] and age at menarche in females.[46–48] In contrast, another study observed simultaneous heterozygosities at three single-nucleotide polymorphisms in the *HOX* genes in a group of autistic individuals with low digit ratios,[49] which indicates that the digit ratio may be related to the *HOX* genes. Like these, the use of digit ratio as a non-invasive retrospective biomarker for prenatal androgen exposure is controversial;[50] however, many researchers have adopted digit ratio as such.[1,4,13,15–18,40,51–55]

To date, it is well known that there are significant ethnic differences in digit ratio. In one study, the Oriental Han had the highest mean digit ratio, followed by the Caucasian Berbers and Uygurs, with the lowest mean ratios found in the Afro-Caribbean Jamaicans.[56]

Unlike digit ratio, studies have not found a relationship between penis size and race.[57] However, there is considerable evidence that normal stretched penile length varied between ethnic groups.[35,58–60] Among various ethnic groups, East Asians have slightly shorter stretched penile length when compared with other ethnic groups (Caucasian and African-American).[35,58–60]

Furthermore, to date, there have been few studies that reveal why men who undergo a normal puberty have different penile lengths. Interestingly, one study in Bulgaria observed that the average penis is bigger at birth and also at the end of sexual maturation in rural populations compared with urban populations.[61] These data indicate that penile size at birth may be associated with penile size after puberty, and that prenatal androgen may have some influence on adult penile size.

Therefore, we hypothesized that the penile length differences between East Asians and other ethnicities may be the result of genetic differences and that the penile length differences between individuals in the same ethnic group may come from the differences of the milieu *in utero*, and we further considered the possibility that digit ratio might be related to penile length.

Among the many studies involving measurement of penile size, several reports have shown correlations between penile length and other somatometric parameters. To date, two studies have shown a correlation between height and penile length.[62,63] Like those studies, the present study showed that flaccid penile length was positively correlated with height. Furthermore, the univariate and multivariate analyses showed that only height was a significant predictive factor for flaccid penile length (**Table 3**). However, in the present study, stretched penile length was not correlated with height but was negatively correlated with digit ratio (**Table 3**).

Two previous studies found correlations between the length of the second digit (index finger) and penile length.[63,64] The present study does not support these findings; neither the length of the second digit nor the length of the fourth digit correlated with flaccid or stretched penile length (**Table 3**). However, the results of our univariate and multivariate analyses did show that stretched penile length correlated with digit ratio (**Table 3**), as men with a lower digit ratio tended to have a longer penile length (**Figure 1**). This means that it is not finger length but digit ratio that can predict adult penile length.

In the present study, penile ratio was negatively correlated with flaccid penile length (**Table 3**). These results indicate that elasticity of a small flaccid penis is higher than that of a large flaccid penis. This supports assertions by Masters and Johnson[65] that a longer flaccid penis is not necessarily longer in erection than a shorter flaccid penis.

In the present study, we measured only the fingers of the right hand because there are numerous reports that differences between the sexes in digit ratio are greater on the right hand than on the left, and there are suggestions that the right hand may be more sensitive to the influence of testosterone.[1,4,15,40,54,55]

Several studies have suggested that males with a low digit ratio may be more likely to suppress signs of pain or discomfort, which could lead to the tendency to measure a longer stretched penis length in this group (low digit ratio) compared to the high-digit-ratio group.[51–53] However, in the present study, penile length was measured under anaesthesia, avoiding pain or discomfort when the penis was fully stretched. Therefore, penile length measurement in our study was not influenced by pain perception.

It is also possible that the elasticity of soft tissues is influenced by prenatal testosterone and that age differences may explain some variation in penile length because penile extensibility decreases with age owing to the loss of elasticity of the tunica albuginea.[66,67] However, in our data, there was no relationship between age and penile length (flaccid penile length: $r=0.066$, $P=0.430$; stretched penile length: $r=0.051$, $P=0.542$) (**Table 3**). Therefore, penile length may not be influenced by penile extensibility that decreases with age as a result of loss of elasticity of the tunica albuginea. These findings are similar to the results of Wessells *et al.*[36]

One limitation of our study is that it is not based on a normal population; rather, participants were recruited from among patients who were hospitalized for urological surgery at a single tertiary academic centre. Nevertheless, we assert that our results present sufficient evidence that a relationship exists between digit ratio and adult penile length, as we excluded patients with conditions known to have a strong influence on penile length.

Another limitation of this study is that we measured stretched penile length, not erectile penile length. However, many studies have reported a strong correlation between stretched penile length and erectile penile length and shown that stretched penile length provides a reliable estimate of the potential maximal elongation during erection.[36,64,68–71] Therefore, the technique applied here for stretched penile length measurement is highly recommended for accurate prediction of erect penile length.[69]

During the foetal period, high concentrations of testosterone lead to high testicular activity, resulting in a lower digit ratio. In the present study, patients with a lower digit ratio tended to have a longer stretched penile length. Stretched penile length was negatively associated with digit ratio. Based on this evidence, we suggest that digit ratio can predict adult penile size and that the effects of prenatal testosterone may in part explain the differences in adult penile length.

AUTHOR CONTRIBUTIONS

IHC designed the study and acquired the data; KHK performed statistical analysis and helped to draft the manuscript; HJ acquired the data; SJY interpreted the data; SWK critically revised the manuscript for important intellectual content; TBK critically revised the manuscript for important intellectual content and helped to draft the manuscript.

COMPETING FINANCIAL INTERESTS

The authors have no financial or any other conflict of interest to declare regarding the contents of this article.

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