Asian Journal of Andrology (2014) 16, 478–481

www.asiaandro.com; www.ajandrology.com

Open Access

ORIGINAL ARTICLE

Male Endocrinology

Relationships among androgen receptor CAG repeat polymorphism, sex hormones and penile length in Han adult men from China: a cross-sectional study

Yan-Min Ma[1,2,*], Kai-Jie Wu[1,*], Liang Ning[1], Jin Zeng[1], Bo Kou[1,2], Hong-Jun Xie[1,2], Zhen-Kun Ma[1,2], Xin-Yang Wang[2], Yong-Guang Gong[1], Da-Lin He[1,2]

This study aimed to investigate the correlations among androgen receptor (AR) CAG repeat polymorphism, sex hormones and penile length in healthy Chinese young adult men. Two hundred and fifty-three healthy men (aged 22.8 ± 3.1 years) were enrolled. The individuals were grouped as CAG short (CAG_S) if they harbored repeat length of ≤20 or as CAG long (CAG_L) if their CAG repeat length was >20. Body height/weight, penile length and other parameters were examined and recorded by the specified physicians; CAG repeat polymorphism was determined by the polymerase chain reaction (PCR) method; and the serum levels of the sex hormones were detected by radioimmunoassay. Student's *t*-test or linear regression analysis was used to assess the associations among AR CAG repeat polymorphism, sex hormones and penile length. This investigation showed that the serum total testosterone (T) level was positively associated with the AR CAG repeat length ($P = 0.01$); whereas, no significant correlation of T or AR CAG repeat polymorphism with the penile length was found ($P = 0.593$). Interestingly, an inverse association was observed between serum prolactin (PRL) levels and penile length by linear regression analyses ($\beta = -0.024$, $P = 0.039$, 95% confidence interval (CI): −0.047, 0). Collectively, this study provides the first evidence that serum PRL, but not T or AR CAG repeat polymorphism, is correlated with penile length in the Han adult population from northwestern China.

Asian Journal of Andrology (2014) **16,** 478–481; doi: 10.4103/1008-682X.124560; published online: 28 February 2014

Keywords: androgen receptor; CAG repeat; testosterone; prolactin; penile length

INTRODUCTION

Sex hormones, such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), estrogen (E_2) and prolactin (PRL), have been identified as potential factors contributing to the formation of the penis during human pregnancy.[1,2]

Of all the sex hormones, T is prominent and has been well-studied.[3–5] Hypogonadism, which is a medical term for the decreased functional activity of the gonads that results in lower levels of serum T, is frequently associated with a small penis or abnormal penile development during childhood and can be partially reversed by T treatment in clinic.[6–8] However, it is still unknown why healthy adult men with normal T levels have different penile lengths and what factors are responsible for the fact that lower T levels are not always associated with a small penis size.

It has been reported that T executes its biological function through the androgen receptor (AR) signaling pathway. AR has a variable NH_2-terminal domain that contains two functionally polymorphic microsatellites, one of which is a polyglutamine tract encoded by CAG repeats. A linear increase of CAG repeat length is associated with the gradual decrease of AR transactivation activity and transcriptional potential.[9]

Because some polymorphic variations of AR alter androgen sensitivity,[9] one hypothesis to explain the variation in penile length in healthy adult men with similar circulating T levels is due to differences in the AR CAG repeat polymorphism. However, there are still no systemic investigations that have determined whether sex hormones or the AR CAG repeat polymorphism affect the final penile length in healthy adult men. Therefore, in the present study, we enrolled 253 healthy young adult men to examine the correlations among the AR CAG repeat polymorphism, sex hormones and penile length.

MATERIALS AND METHODS

Participants

A total of 253 healthy young adult men (age: 22.8 ± 3.1 years; height: 171.39 ± 5.86 cm; body mass: 64.43 ± 10.09 kg; mean ± standard deviation (s.d.)) were enrolled in this study. They were recruited among students from four universities or colleges in Xi'an, Shaanxi Province, People's Republic of China. The physical condition of each participant was determined by his medical history and physical examination. Subjects who were receiving medication or had any chronic diseases were excluded. The study was approved by the Ethical Committee of the Xi'an Jiaotong University, and all of the volunteers provided their written consent before participation.

[1]Department of Urology, First Affiliated Hospital of Medical School, Xi'an Jiaotong University, Xi'an; [2]Oncology Research Lab, Key Laboratory of Environment and Genes Related to Diseases, Ministry of Education of the People's Republic of China, Xi'an, China.
*These authors contributed equally to this work.
Correspondence: Dr. YG Gong (gyg0207@sina.com) or Dr. DL He (dalinhexjtu@126.com)
Received: 05 August 2013; Revised: 23 September 2013; Accepted: 27 November 2013

Criteria for measuring the penile length

Procedures for penile measurement have been described previously.[10] Briefly, under room temperature conditions, the penile length was measured by a Vernier caliper along the dorsum of the penis from the pubopenile junction to the tip of the glans at maximal extension, and each measurement was repeated three times.

Blood collection and DNA extraction

Considering that the AR gene may be affected by ethnicity, five minorities (2%) were excluded from the analysis. Briefly, 5 ml fasting blood from an antecubital vein was collected between 8:00 and 9:00 am and immediately separated into the plasma, red blood cells and buffy coat. Afterwards, DNA was extracted from the buffy coat (leukocyte) using the Qiagen QIAamp blood kit and following the manufacturer's recommendations (Qiagen, Chatsworth, CA, USA).

Serum sex hormone determination

The plasma obtained from the blood was used for the determination of sex hormones. Hormones, including FSH, LH, PRL, T, E_2 and progesterone, were detected by radioimmunoassay (Tianjin Jiuding Medical Bio-Engineering Co. Ltd, Tianjin, China). For the FSH, LH, PRL, T, E_2 and progesterone assays, the functional sensitivities were 1 mIU ml^{-1}, 0.9 mIU ml^{-1}, 0.9 ng ml^{-1}, 1 ng ml^{-1}, 2 pg ml^{-1} and 0.03 ng ml^{-1}, respectively, with intra- and interassay coefficient of variation at 5.5% and 8.7%, 5.4% and 8.7%, 5.4% and 9.3%, 7.4% and 9.8%, 7.7% and 8.9%, and 7.2% and 8.9%, respectively.

CAG repeat polymorphism

The method for analyzing the CAG repeat polymorphism in the AR gene has been described in detail previously.[11,12] Briefly, exon 1 of the AR gene was amplified using the forward 5'-TCCAGAATCTGTTCCAGAGCGTGC-3' and reverse 5'-GCTGTG-AAGGTTGCTGTTCCTCAT-3' primers flanking the CAG repeat. One of the primers was marked with Cy5.5 fluorescent dye. Amplification was performed in a 25 μl reaction volume containing 50 ng of genomic DNA and 200 μmol l^{-1} of each deoxynucleotide triphosphate. The concentration of the primer was 1.2 μmol l^{-1}. PCR conditions were set as follows: 30 cycles of 95°C for 45 s, 56°C for 30 s and 72°C for 30 s for amplification. The PCR program was initiated with a denaturation step at 95°C for 5 min and terminated with an extension step at 72°C for 5 min.[13] The PCR products were analyzed on a Genescan-run ABI 377 DNA gel-slab electrophoresis sequencer (Perkin-Elmer, Co, Norwalk, CT, USA) with a TAMRA-labeled internal length standard (Genescan-500 TAMRA, Applied Biosystems, Foster City, CA, USA). Genotyper software was used to determine the genotypes (Genotyper version 2.0, Applied Biosystems).[14]

Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (version 13.0, SPSS Inc., Chicago, IL, USA). All descriptive data are expressed as the mean ± s.d. The correlation between the AR CAG repeat polymorphism or the sex hormones and the penile length were determined. Taking the AR CAG repeat length as dichotomous variables with allele cutoff thresholds, the individuals were grouped as CAG short (CAG_S) if harboring repeats of ≤20 and CAG long (CAG_L) if harboring repeats of >20. Student's *t*-tests were used to compare the two groups if the distribution was approximately normal.[13] Due to the normal distribution of the penile length by the Kolmogorov-Smirnov test, linear regression analysis was used to assess the independence of associations between penile length and the other variables. The results were expressed using the regression coefficient (β), significance value (*P*) and the 95% confidence intervals (CI) for each calculation. All statistical tests were two-sided and $P < 0.05$ was considered statistically significant.

RESULTS

AR CAG repeat polymorphism

The subjects' penile lengths and hormone statuses are shown in **Table 1**. In our study, the AR CAG repeat polymorphism ranged from 13 to 30, with an approximately normal distribution similar to those of previous studies in the Chinese population.[12] The mean was 20.55 and the median was 20 (**Figure 1**).

Sex hormones and AR CAG repeat polymorphism

The correlation between AR CAG repeat polymorphism and sex hormones is still controversial.[15–23] In our study, out of all sex hormones, the serum T concentration was 12.5% higher in the CAG_L group compared to the CAG_S group (25.6 ± 6.98 and 28.8 ± 7.72 nmol l^{-1}, respectively), and this difference reached statistical significance ($P = 0.01$). However, no significant correlation was found between AR CAG polymorphisms and the levels of FSH, LH, PRL, E_2 or progesterone (P = 0.88, 0.89, 0.62, 0.69 and 0.61, respectively) (**Table 1**).

AR CAG repeat polymorphism and penile length

Previous studies have shown that the AR CAG repeat length was negatively correlated with AR transactivation activity.[24,25] Thus, we wanted to investigate whether AR CAG repeat polymorphism were able to affect the final penile length of adult men. After statistical analysis, despite the numerically longer penile length in the CAG_S group than in the CAG_L group, the difference did not reach statistical significance (10.2 ± 1.46 and 10.1 ± 1.28 cm, respectively, P = 0.59) (**Table 1**).

Table 1: Age, penile length and sex hormones in men with AR CAG_S and CAG_L polymorphisms

	CAG_S (n=126, mean±s.d.)	CAG_L (n=122, mean±s.d.)	*P* value
Age (year)	22.9±3.6	22.7±2.6	0.52
Penile length (cm)	10.2±1.5	10.1±1.3	0.59
FSH (IU l^{-1})	7.3±2.0	7.4±2.4	0.88
LH (IU l^{-1})	9.4±2.5	9.3±2.5	0.89
PRL (μg l^{-1})	15.6±12.7	16.5±10.4	0.62
Total T (nmol l^{-1})	25.6±7.0	28.8±7.7	0.01
Total E_2 (pmol l^{-1})	390.7±93.6	397.2±101.9	0.69
Progesterone (nmol l^{-1})	1.14±0.5	1.18±0.6	0.61

E_2: estrogen; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin; T: testosterone; s.d.: standard deviation

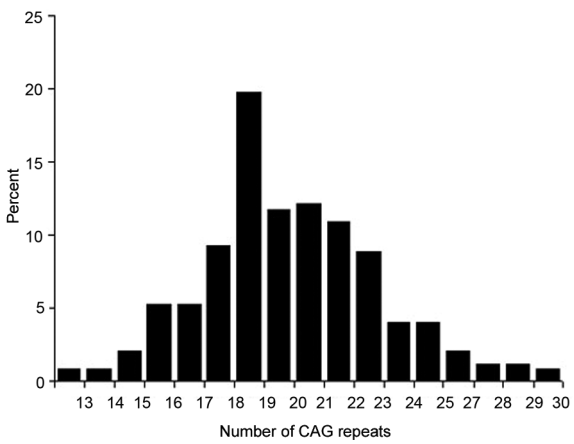

Figure 1: Percent distribution of the number of AR CAG repeats.

Linear regression analysis

The penile length was set as the dependent variable, and the AR CAG repeat polymorphism, sex hormones, body mass index and waist/hip ratios were set as the independent variables. As shown in **Table 2**, PRL was the only factor found to be significant after statistical analysis ($\beta = -0.024$, $P = 0.039$, 95% CI: − 0.047, 0).

Considering that 42 out of the 248 participants had serum PRL levels exceeding the maximum value of the normal reference, individuals were grouped as PRL_N (normal) if they harbored a concentration of <20 $\mu g l^{-1}$ and as PRL_H (high) if they harbored a concentration of ≥20 $\mu g l^{-1}$. As shown in **Figure 2**, a statistically significant decrease in the penile length was observed in the PRL_H group compared with the PRL_N group after the *t*-test analysis (PRL_N *vs* PRL_H, 10.3 ± 1.4 *vs* 9.8 ± 1.1 cm, $P = 0.025$).

DISCUSSION

The goal of this study was to investigate the correlations among AR CAG repeat polymorphism, sex hormones and penile length in healthy young adult men from China. In total, we made two major new discoveries: (i) AR CAG repeat polymorphism have no relationship with human penile length and (ii) human serum PRL levels negatively correlate with penile length.

Our study first showed that the AR CAG repeat length was dramatically correlated with the total levels of serum T, but not with the levels of serum FSH, LH, PRL, E_2 or P. Similar results have been reported in several previous publications,[15–19] although some of the results are controversial.[20–23] For example, Stanworth *et al.*[26,27] showed that longer AR CAG repeats correlated with higher T and LH levels in men with type 2 diabetes and explained that less active AR with longer AR CAG produced less suppression of the LH release. Thereby, LH levels were increased, and higher T levels were stimulated.[26,27] However, Huhtaniemi *et al.*[17] conducted a multinational prospective cohort observational study and showed that CAG repeats were obviously correlated with total T but not with LH. One of their explanations was that the concomitant increase of circulating T levels in men with longer repeats could adequately compensate for the lower AR activity in order to prevent the apparent deficiency of androgen action. Skrgatic *et al.*[18] also reported a positive correlation between the CAG repeats and total T levels in polycystic ovary syndrome. However, Andersen *et al.*[20] showed that there was no significant correlation between the AR CAG repeat length and the total T, E_2, FSH or LH levels.

Table 2: Linear regression analysis for the associations between penile length and other variables. Regression coefficients (β), significance values (*P*) and 95% confidence intervals (CI) were calculated for the estimates[a]

Model	*Unstandardized coefficients β*	*P value*	*95% CI for β*
(Constant)	12.373		(8.354, 16.392)
FSH	0.007	0.911	(-0.113, 0.127)
LH	0.013	0.840	(-0.113, 0.139)
PRL	–0.024	0.039	(–0.047, 0)
T	–0.016	0.337	(–0.050, 0.017)
E_2	–0.001	0.318	(–0.004, 0.001)
Progesterone	0.066	0.767	(–0.374, 0.506)
$CAG_{(n)}$	0.010	0.785	(–0.064, 0.084)
BMI	0.052	0.352	(–0.058, 0.162)
Waist/hip ratio	–2.977	0.223	(–7.788, 1.833)

BMI: body mass index; $CAG_{(n)}$: CAG repeats; E2: estrogen FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin; T: testosterone. [a]Dependent variable: penile length

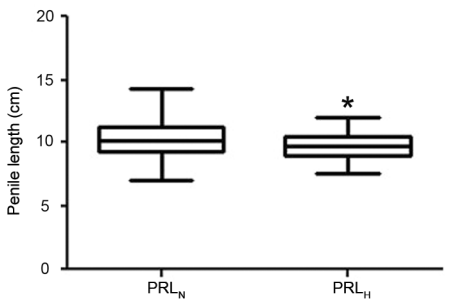

Figure 2: Penile length in the PRL_N and PRL_H groups. The box plots show the average penile lengths for the PRL levels in the PRL_N and PRL_H groups. PRL_N and PRL_H (with*) indicate normal and high levels of PRL, respectively. PRL_H: prolactin (high); PRL_N: prolactin (normal).

As previously described, the AR gene contains a great number of CAG repeats, which could result in various polyglutamine tracts. Longer polyglutamine tracts could cause a reduced transcriptional activation of AR.[24,25] Previous reports described ambiguous results regarding the association between expanded CAG repeat polymorphism and micropenis in the Japanese.[24,28] However, our results indicated that the genotype of CAG repeat polymorphism has no discernible effect on penile length. It is likely that the expansion of CAG repeats can be detected as a positive modifying factor in one population but not in another. However, individuals with longer AR CAG repeat length usually exhibit higher serum T levels. To a certain extent, the reduced effect of AR transactivation could be relieved by higher T concentrations. This is a likely explanation for why CAG repeat polymorphism had no discernible effect on the ultimate human penile length in our study.

Interestingly, a negative correlation between the serum PRL levels and penile length was detected in our study. PRL is viewed as a classical endocrine hormone that is not just produced by pituitary lactotroph cells but is also secreted by several tissues, including the mammary glands, prostate, brain, some immune cells and others.[29] Various actions of PRL have been reported, including its effects on water and salt balance,[30] growth and development,[29] endocrinology and metabolism,[31,32] brain and behaviour,[33–35] reproduction[29,36] and immune regulation.[37,38] Pathological hyperprolactinemia has been reported to result in galactorrhea oligo/amenorrhea in women, impotence in men and loss of libido and infertility in both sexes.[39] PRL receptor-deficient animals have shown an almost complete failure to lactate, infertility in females and delayed fertility in males.[40] Furthermore, Bartke *et al.*[41] showed that PRL could modulate responses to the negative steroid feedback at the pituitary level and reported that both LH and T levels were reduced in hyperprolactinemic men. Similar results have reported that long-term hyperprolactinemia could cause the suppression of the hypothalamic-pituitary gonadal axis and a decrease in the levels of gonadotropin-releasing hormone, LH and T in males.[42] Recently, Roke *et al.*[43] reported that boys with antipsychotic-induced hyperprolactinemia had obviously lower T levels than male adolescents with normal PRL levels. Therefore, we supposed that higher levels of PRL suppressed the hypothalamic-pituitary-gonadal axis and decreased T levels, resulting in an inhibitory effect on penile growth.

In summary, this report presents evidence that men with longer AR CAG repeats had higher T levels that could compensate partly or totally for the weaker activity of AR. Furthermore, men with longer AR CAG repeats do not necessarily have shorter penile lengths. This may be due to the equilibrium between AR CAG repeats and T levels. A promising and important finding of this study was the presence of higher PRL levels in healthy adult men with shorter penile lengths; we are the first to report this discovery. These findings have potential

implications for the interpretation of epidemiological studies, the diagnosis of hypogonadism in borderline situations and possibly the individualization of micropenis therapies in men.

AUTHOR CONTRIBUTIONS

YMM and KJW participated in the design of the trial, conducted the data acquisition, interpreted and statistically analyzed the data and drafted the manuscript. LN and JZ designed the study and offered the study materials. HJX and ZKM conducted the data acquisition, interpreted and statistically analyzed the data. BK and XYW conducted the data acquisition. YGG and DLH designed the study, interpreted the data and drafted the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ACKNOWLEDGMENTS

This study was partially supported by the National Natural Science Foundation of China (NSFC 81270688 to YGG).

REFERENCES

1 Nagasaki K, Katsumata N, Ogawa Y, Kikuchi T, Uchiyama M. Novel C617Y mutation in the 7th transmembrane segment of luteinizing hormone/choriogonadotropin receptor in a Japanese boy with peripheral precocious puberty. *Endocr J* 2010; 57: 1055–60.
2 Cohen-Bendahan CC, van de Beek C, Berenbaum SA. Prenatal sex hormone effects on child and adult sex-typed behavior: methods and findings. *Neurosci Biobehav Rev* 2005; 29: 353–84.
3 Sutherland RS, Kogan BA, Baskin LS, Mevorach RA, Conte F, *et al*. The effect of prepubertal androgen exposure on adult penile length. *J Urol* 1996; 156: 783–7.
4 Boas M, Boisen KA, Virtanen HE, Kaleva M, Suomi AM, *et al*. Postnatal penile length and growth rate correlate to serum testosterone levels: a longitudinal study of 1962 normal boys. *Eur J Endocrinol* 2006; 154: 125–9.
5 Ishii T, Hayashi M, Suwanai A, Amano N, Hasegawa T. The effect of intramuscular testosterone enanthate treatment on stretched penile length in prepubertal boys with hypospadias. *Urology* 2010; 76: 97–100.
6 Kim SO, Ryu KH, Hwang IS, Jung SI, Oh KJ, *et al*. Penile growth in response to human chorionic gonadotropin (HCG) treatment in patients with idiopathic hypogonadotrophic hypogonadism. *Chonnam Med J* 2011; 47: 39–42.
7 Bin-Abbas B, Conte FA, Grumbach MM, Kaplan SL. Congenital hypogonadotropic hypogonadism and micropenis: effect of testosterone treatment on adult penile size why sex reversal is not indicated. *J Pediatr* 1999; 134: 579–83.
8 Tietjen DN, Uramoto GY, Tindall DJ, Husmann DA. Micropenis in hypogonadotropic hypogonadism: response of the penile androgen receptor to testosterone treatment. *J Urol* 1998; 160: 1054–7.
9 Chamberlain NL, Driver ED, Miesfeld RL. The length and location of CAG trinucleotide repeats in the androgen receptor N-terminal domain affect transactivation function. *Nucleic Acids Res* 1994; 22: 3181–6.
10 Khan S, Bhaskar S, Lam W, Donat R. Establishing a reference range for penile length in Caucasian British men: a prospective study of 609 men. *BJU Int* 2012; 109: 740–4.
11 Bharaj BS, Vassilikos EJ, Diamandis EP. Rapid and accurate determination of (CAG) n repeats in the androgen receptor gene using polymerase chain reaction and automated fragment analysis. *Clin Biochem* 1999; 32: 327–32.
12 Hsing AW, Gao YT, Wu G, Wang X, Deng J, *et al*. Polymorphic CAG and GGN repeat lengths in the androgen receptor gene and prostate cancer risk: a population-based case-control study in China. *Cancer Res* 2000; 60: 5111–6.
13 Guadalupe-Grau A, Rodriguez-Gonzalez FG, Ponce-Gonzalez JG, Dorado C, Olmedillas H, *et al*. Bone mass and the CAG and GGN androgen receptor polymorphisms in young men. *PLoS ONE* 2010; 5: e11529.
14 Wedren S, Magnusson C, Humphreys K, Melhus H, Kindmark A, *et al*. Associations between androgen and Vitamin D receptor microsatellites and postmenopausal breast cancer. *Cancer Epidemiol Biomarkers Prev* 2007; 16: 1775–83.
15 Krithivas K, Yurgalevitch SM, Mohr BA, Wilcox CJ, Batter SJ, *et al*. Evidence that the CAG repeat in the androgen receptor gene is associated with the age-related decline in serum androgen levels in men. *J Endocrinol* 1999; 162: 137–42.
16 Crabbe P, Bogaert V, De Bacquer D, Goemaere S, Zmierczak H, *et al*. Part of the interindividual variation in serum testosterone levels in healthy men reflects differences in androgen sensitivity and feedback set point: contribution of the androgen receptor polyglutamine tract polymorphism. *J Clin Endocrinol Metab* 2007; 92: 3604–10.
17 Huhtaniemi IT, Pye SR, Limer KL, Thomson W, O'Neill TW, *et al*. European Male Ageing Study Group. Increased estrogen rather than decreased androgen action is associated with longer androgen receptor CAG repeats. *J Clin Endocrinol Metab* 2009; 94: 277–84.
18 Skrgatic L, Baldani DP, Cerne JZ, Ferk P, Gersak K. CAG repeat polymorphism in androgen receptor gene is not directly associated with polycystic ovary syndrome but influences serum testosterone levels. *J Steroid Biochem Mol Biol* 2012; 128: 107–12.
19 Walsh S, Zmuda JM, Cauley JA, Shea PR, Metter EJ, *et al*. Androgen receptor CAG repeat polymorphism is associated with fat-free mass in men. *J Appl Physiol (1985)* 2005; 98: 132–7.
20 Andersen ML, Guindalini C, Santos-Silva R, Bittencourt LR, Tufik S. Androgen receptor CAG repeat polymorphism is not associated with erectile dysfunction complaints, gonadal steroids, and sleep parameters: data from a population-based survey. *J Androl* 2011; 32: 524–9.
21 Zitzmann M, Brune M, Kornmann B, Gromoll J, von Eckardstein S, *et al*. The CAG repeat polymorphism in the AR gene affects high density lipoprotein cholesterol and arterial vasoreactivity. *J Clin Endocrinol Metab* 2001; 86: 4867–73.
22 Van Pottelbergh I, Lumbroso S, Goemaere S, Sultan C, Kaufman JM. Lack of influence of the androgen receptor gene CAG-repeat polymorphism on sex steroid status and bone metabolism in elderly men. *Clin Endocrinol (Oxf)* 2001; 55: 659–66.
23 Alevizaki M, Cimponeriu AT, Garofallaki M, Sarika HL, Alevizaki CC, *et al*. The androgen receptor gene CAG polymorphism is associated with the severity of coronary artery disease in men. *Clin Endocrinol (Oxf)* 2003; 59: 749–55.
24 Lim HN, Chen H, McBride S, Dunning AM, Nixon RM, *et al*. Longer polyglutamine tracts in the androgen receptor are associated with moderate to severe undermasculinized genitalia in XY males. *Hum Mol Genet* 2000; 9: 829–34.
25 Yu H, Bharaj B, Vassilikos EJ, Giai M, Diamandis EP. Shorter CAG repeat length in the androgen receptor gene is associated with more aggressive forms of breast cancer. *Breast Cancer Res Treat* 2000; 59: 153–61.
26 Stanworth RD, Kapoor D, Channer KS, Jones TH. Dyslipidaemia is associated with testosterone, oestradiol and androgen receptor CAG repeat polymorphism in men with type 2 diabetes. *Clin Endocrinol (Oxf)* 2011; 74: 624–30.
27 Stanworth RD, Kapoor D, Channer KS, Jones TH. Androgen receptor CAG repeat polymorphism is associated with serum testosterone levels, obesity and serum leptin in men with type 2 diabetes. *Eur J Endocrinol* 2008; 159: 739–46.
28 Ishii T, Sato S, Kosaki K, Sasaki G, Muroya K, *et al*. Micropenis and the AR Gene: mutation and CAG repeat-length analysis. *J Clin Endocrinol Metab* 2001; 86: 5372–8.
29 Bernichtein S, Touraine P, Goffin V. New concepts in prolactin biology. *J Endocrinol* 2010; 206: 1–11.
30 Breves JP, Seale AP, Helms RE, Tipsmark CK, Hirano T, *et al*. Dynamic gene expression of GH/PRL-family hormone receptors in gill and kidney during freshwater-acclimation of Mozambique tilapia. *Comp Biochem Physiol A Mol Integr Physiol* 2011; 158: 194–200.
31 Clapp C, Martínez de la Escalera L, Martínez de la Escalera G. Prolactin and blood vessels: a comparative endocrinology perspective. *Gen Comp Endocrinol* 2012; 176: 336–40.
32 Davis JR. Prolactin and reproductive medicine. *Curr Opin Obstet Gynecol* 2004; 16: 331–7.
33 Larsen CM, Grattan DR. Prolactin, neurogenesis, and maternal behaviors. *Brain Behav Immun* 2012; 26: 201–9.
34 Takayanagi Y, Onaka T. Roles of prolactin-releasing peptide and RFamide related peptides in the control of stress and food intake. *FEBS J* 2010; 277: 4998–5005.
35 Walters J, Jones I. Clinical questions and uncertainty–prolactin measurement in patients with schizophrenia and bipolar disorder. *J Psychopharmacol* 2008; 22: 82–9.
36 Egli M, Leeners B, Kruger TH. Prolactin secretion patterns: basic mechanisms and clinical implications for reproduction. *Reproduction* 2010; 140: 643–54.
37 Clevenger CV, Freier DO, Kline JB. Prolactin receptor signal transduction in cells of the immune system. *J Endocrinol* 1998; 157: 187–97.
38 Velkeniers B, Dogusan Z, Naessens F, Hooghe R, Hooghe-Peters EL. Prolactin, growth hormone and the immune system in humans. *Cell Mol Life Sci* 1998; 54: 1102–8.
39 Molitch ME, Thorner MO, Wilson C. Management of prolactinomas. *J Clin Endocrinol Metab* 1997; 82: 996–1000.
40 Bole-Feysot C, Goffin V, Edery M, Binart N, Kelly PA. Prolactin (PRL) and its receptor: actions, signal transduction pathways and phenotypes observed in PRL receptor knockout mice. *Endocr Rev* 1998; 19: 225–68.
41 Bartke A, Matt KS, Steger RW, Clayton RN, Chandrashekar V, *et al*. Role of prolactin in the regulation of sensitivity of the hypothalamic-pituitary system to steroid feedback. *Adv Exp Med Biol* 1987; 219: 153–75.
42 Roke Y, van Harten PN, Boot AM, Buitelaar JK. Antipsychotic medication in children and adolescents: a descriptive review of the effects on prolactin level and associated side effects. *J Child Adolesc Psychopharmacol* 2009; 19: 403–14.
43 Roke Y, van Harten PN, Buitelaar JK, Tenback DE, de Rijke YB, *et al*. Antipsychotic-induced hyperprolactinemia and testosterone levels in boys. *Horm Res Paediatr* 2012; 77: 235–40.

How to cite this article: Ma YM, Wu KJ, Ning L, Zeng J, Kou B, Xie HJ, Ma ZK, Wang XY, Gong YG, He DL. Relationships among androgen receptor CAG repeat polymorphism, sex hormones and penile length in Han adult men from China: a cross-sectional study. *Asian J Androl* 28 February 2014. doi: 10.4103/1008-682X.124560. [Epub ahead of print]