

The role of anogenital distance in the incidence risk of prostate cancer in China

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Research Article

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Abstract

Background: Anogenital distance (AGD) can be used as a biomarker to indirectly indicate androgen levels during the sexual maturation of mammals. In order to gain a deeper understanding of the association between the AGD and the risk of prostate cancer (PCa), we performed this study

Materials: A total of 107 patients undergoing perineal prostate biopsy from November 2019 to August 2020 were enrolled. All patients diagnosed 57 PCa patients and 50 benign prostatic hyperplasia (BPH) patients through perineal prostate biopsy in our hospital. The anus to the posterior base of the scrotum (AGDAS) and the cephalad insertion of the penis (AGDAP) of all patients were measured before prostate biopsy.

Result: The mean age of patients with PCa was 69.46 ± 7.52 and the mean age of patients with BPH was 67.38 ± 8.26 . We did not find a significant association between age and BMI in the risk of PCa (all $p > 0.05$). Besides, there was no significant association between AGD and the risk of PCa ($p > 0.05$). We only discovered that PSA could play an important role in the development of PCa.

Conclusion: AGD may not play an important role in predicting the incidence risk of PCa. We still need a large-scale prospective study to explore the true association between AGD and the incidence of PCa.

Introduction

Prostate cancer (PCa) is currently one of the most common male malignancies in Western countries [1]. Although the current incidence rate of PCa in Asian countries is lower than in western countries, the incidence and mortality rates of PCa have been increasing in China and other Asian countries [2]. The distance from the anus to the genitals is defined as the anogenital distance (AGD), which indirectly represents the development of mammalian secondary sexual features and the level of androgen exposure in the body. And the AGD of males is longer than that of females [3]. Some animal studies had shown that the AGD was formed in mammals in the uterus and continue to develop during adulthood, which indicated that the AGD was closely related to androgen exposure [4–5]. Serum testosterone level is an important factor in promoting the normal growth and development of prostate glands, so prostate glands are highly sensitive to androgens [6]. Some review studies had also found that a high level of serum testosterone may increase the risk of PCa [7–8]. Castaño-Vinyals et al demonstrated that PCa patients had shorter AGD than the control group [9]. Therefore, we conducted this study to further explore the relationship between the AGD and the risk of PCa in the Chinese population.

Materials And Methods

Patient selection from November 2019 to August 2020, 107 patients who underwent transperineal prostate biopsy in Tianjin Medical University. All patients were underwent prostate biopsy due to PSA ≥ 2.5 ng/ml. There were 50 patients diagnosed with benign prostatic hyperplasia (BPH) and 57 patients had PCa. Anogenital distance from the anus to the upper penis (AGD_{AP}) and anogenital distance from the

anus to the scrotum(AGD_{AS}) were measured according to with Swan et al[10]. Subjects were measured AGD varies by digital caliper when his thighs was forming an angle of 45° with the examination table, Each patient measures the AGD three times and takes the average value of the three measurements. Adjustment for AGD value of different patients through BMI.

Statistical Analysis

We used SPSS.22 to statistically analyze the data, used mean \pm SD to represent continuous variables, chi-square test to compare binary variables. Univariate and multivariate logistic regression analysis were used to select the independent risk factors for the incidence of PCa. All $p < 0.05$ is considered statistically different.

Results

We had included 107 patients who underwent transperineal prostate biopsy between November 2019 to August 2020. In those patients, 57 patients were diagnosed with PCa and 50 patients were diagnosed with BPH. The mean age of PCa patients was 69.46 ± 7.52 years, and the mean age of BPH patients was 67.38 ± 8.26 years respectively. Age and BMI are not statistically different in PCa and BPH(all $p \geq 0.05$). There was no significant difference in AGDAP and AGDAS between PCa group and the BPH group(all $p \geq 0.05$). Similarly, we also found adjusted AGDAP and adjusted AGDAS were not significant between PCa group and BPH group(all $p \geq 0.05$). Patients with PCa had higher PSA levels than patients with BPH($p \leq 0.001$)(Table 1).

Table 1
Characteristics of the study participants and anogenital distances

	Prostate cancer(n = 57)	BPH(n = 50)	P
Age(years)	69.46 ± 7.52	67.38 ± 8.26	0.177
PSA, no(%)			0.001*
<10ng/ml	12(21%)	29(58%)	
≥ 10ng/ml	45(79%)	21(42%)	
BMI(kg/m ²)	25.41 ± 4.22	24.56 ± 3.28	0.253
AGD _{AP} (cm)	11.41 ± 1.18	11.1 ± 1.15	0.169
AGD _{AS} (cm)	3.02 ± 0.79	3.15 ± 0.94	0.463
Adjusted AGD _{AP} (AGD _{AP} /BMI)	0.46 ± 0.06	0.46 ± 0.07	0.913
Adjusted AGD _{AS} (AGD _{AS} /BMI)	0.12 ± 0.03	0.13 ± 0.04	0.243
AGD AP, anogenital distance from anus to upper penis; AGD AS, anogenital distance from anus to scrotum. *Statistically significant.			
AGD AP, anogenital distance from anus to upper penis; AGD AS, anogenital distance from anus to			
Scrotum; BMI, body mass index;			

Discussion

To verify whether there is a clear relationship between the AGD and the incidence of PCa, we conducted this study. Studies have shown that the AGD is an external manifestation of the level of androgen exposure in the body, and during the development of the sexual characteristics of mammals, the AGD which presents prenatal androgen exposure is longer in men than in women[11]. Sahin et al found that AGD was related to the risk of PCa, their results found that the PCa patients had longer AGDAP compared to the control group[12]. Besides, Maldonado-Carceles et al published their research in 2016 and suggested that patients with longer AGDAS might have higher biopsy Gleason score and there was no obvious correlation between AGDAP and the severity of biopsy Gleason score[13]. Some literature showed that the level of testosterone was significant correlated with the occurrence of PCa[14–15]. Patients with PCa may have higher prenatal androgen levels than BPH. Some studies had also found that there is a link between AGD and testosterone levels in men and women[16–17]. A longer AGD indicates that the human has more prenatal androgen exposure levels. Current researchers believed that the development of normal prostate depended on androgen[18–19]. As such, it may affect the proliferation of testicular stromal cells, leading to higher androgen during adolescence. This also shows that longer AGD can lead to increased androgen levels in adulthood, leading to an increased risk and severity of PCa.

While Boyle et al performed a meta-analysis and concluded that PCa appeared to be unrelated to endogenous testosterone levels[20]. And the occurrence and development of PCa are independent of serum testosterone levels. However, Castañ o-Vinyals et al collected 111 patients, of which 60 were PCa patients[11]. In their conclusion, they proposed for the first time that AGD was related to the risk of PCa, and that PCa patients had shorter AGDAP compared to the control group. In our research, we had not found a significant relationship between the AGD and the risk of PCa($p \geq 0.05$), and the AGD adjusted by BMI also had no obvious association between the PCa group and BPH group($p \geq 0.05$). The relationship between testosterone and PCa is not easy to identify, because it is difficult to predict the current testosterone level in clinical practice. The personal testosterone level fluctuates throughout the day and may be affected by the environment, diet, and so on. Garc í a-Cruz et al invested that lower testosterone levels had indicated poor prognosis and advanced PCa[21]. Thus, there was no clear relationship between the level of testosterone and the progression of PCa. In many studies, the measured AGDAP is associated with pre-pregnancy androgen exposure and the risk of PCa[22, 12]. while AGDAS measurement is related to male reproductive ability and reproductive hormones[23]. So for now, AGD is related to content in many fields, but it is still in the exploratory stage. Therefore, there was no identified result for the relationship between AGD and the incidence of PCa. We still needed a large multi-center study to explore the relationship between anogenital distance and the risk of PCa.

Limitation

First of all, the number of patients we included in our research was small and the results might be biased. Secondly, when we screened patients, we did not limit the PSA range. Our results found that the PSA of patients with PCa was significantly higher than BPH patients, which may affect the final results.

Conclusion

So far, there is little literature on the relationship between AGD and the incidence of PCa. The relationship between androgen levels and PCa was still controversial. Our research did not find a meaningful relationship between the AGD and the incidence risk of PCa. Further researches need to be designed to verify this hypothesis that whether AGD can be combined with PSA to predict the risk of PCa.

Declarations

Ethics approval

Tianjin Medical University Second Hospital Ethical Review Board have approved this study.

Consent for publication

All authors read and approved the final manuscript

Availability of data and materials

All the data included in this study are presented in this article

Competing interests

There was no conflict of interest.

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Authors' contributions

Conception and Design: JZ and RL; Extraction of Data: JZ; Jiatong Zhou and Ranlu Liu contributed to conception and design; Jiatong Zhou contributed to drafting the article; Ranlu Liu contributed to revising it for intellectual content. All authors read and approved the final manuscript.

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Further information

Not available

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