

·临床研究·

体检男性良性前列腺增大伴前列腺钙化的相关因素

张小马^{1,2}, 肖莉³, 林长明², 张力¹, 周骏¹, 郝宗耀¹, 梁朝朝¹

(1. 安徽医科大学第一附属医院泌尿外科, 安徽合肥 230022; 2. 安徽医科大学第四附属医院泌尿外科, 安徽合肥 230012; 3. 安徽医科大学第四附属医院健康管理中心, 安徽合肥 230012)

摘要:【目的】前列腺钙化(PC)影响良性前列腺增大(BPE)导致的下尿路症状(LUTS),为了BPE者PC的防治提供参考,本研究探讨体检男性BPE伴PC的相关因素。【方法】回顾性分析2018年10月至2021年6月3433名在安徽医科大学第四附属医院体检男性中863例BPE的临床资料,单因素分析比较A组(BPE伴PC)和B组(BPE不伴PC)血、尿等指标参数,Logistic回归分析BPE伴PC的相关因素。【结果】BPE(定义为前列腺体积 ≥ 20 mL)伴PC在BPE者中的发生率为37.5% (324/863)。A组年龄、血尿素氮、尿PH值高于B组($P < 0.05$),身高、体质量、血尿酸低于B组($P < 0.05$),前列腺回声不均者比例高于B组($P < 0.05$),两组间代谢综合征及组分者比例无差异($P > 0.05$)。Logistic回归分析显示前列腺回声不均、尿PH值和年龄(尤其80~89岁)是体检BPE者BPE伴PC的相关因素[OR 95%CI为2.082 (1.111, 3.900); OR 95%CI为1.419 (1.152, 1.747)和OR 95%CI为17.829 (3.224, 98.594)]。【结论】体检BPE者BPE伴PC的发生率较高。除年龄外,前列腺回声不均和尿PH值也是体检BPE者BPE伴PC的相关因素。

关键词:良性前列腺增大;前列腺钙化;健康体检;相关因素

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Related Factors of Benign Prostatic Enlargement with Prostate Calcification in Men Receiving Physical Examinations

ZHANG Xiao-ma^{1,2}, XIAO Li³, LIN Chang-ming², ZHANG Li¹, ZHOU Jun¹,
HAO Zong-yao¹, LIANG Chao-zhao¹

(1. Department of Urology, The First Affiliated Hospital of Anhui Medical University, Hefei 230022, China; 2. Department of Urology, The Fourth Affiliated Hospital of Anhui Medical University, Hefei 230012, China; 3. Department of Health Management Center, The Fourth Affiliated Hospital of Anhui Medical University, Hefei 230012, China)

Correspondence to: LIANG Chao-zhao; E-mail: liang_chaozhao@ahmu.edu.cn

Abstract:【Objective】Lower urinary tract symptoms (LUTS) caused by benign prostatic enlargement (BPE) are influenced by prostate calcification (PC). The aim of this study is to explore the related factors of BPE with PC in men receiving physical examinations, and to provide some references for the prevention and treatment of PC in BPE patients.【Methods】The clinical data of 863 cases of BPE among 3433 men who underwent physical examination in the Fourth Affiliated Hospital of Anhui Medical University from October 2018 to June 2021 were analyzed retrospectively. The blood and urine examination indexes between group A (BPE with PC) and group B (BPE without PC) were compared by univariate analysis. The related factors of BPE with PC were analyzed by logistic regression.【Results】The incidence of BPE (defined as prostate volume ≥ 20 mL) with PC in BPE patients was 37.5% (324 / 863). Univariate analysis showed that age, blood urea nitrogen, and urinary pH value in group A were significantly higher than those in group B ($P < 0.05$), and height,

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作者简介:张小马,硕士,主任医师,研究方向:泌尿男科学,E-mail: zhangxiaoma8@126.com;梁朝朝,通信作者,教授,

E-mail: liang_chaozhao@ahmu.edu.cn

weight and blood uric acid of group A were lower than those of group B group ($P<0.05$). The proportion of patients with inhomogeneous prostatic echo in group A was higher than that in group B ($P<0.05$). There was no significant difference in the proportion of patients with metabolic syndrome and components between the two groups ($P>0.05$). Multivariate logistic regression analysis showed that inhomogeneous echo of the prostate, urinary pH and age (especially 80~89 years old) were the related factors of BPE with PC in BPE patients undergoing checkups [OR 95%CI 2.082 (1.111, 3.900); OR 95%CI 1.419 (1.152, 1.747) and OR 95%CI 17.829 (3.224, 98.594)].

【Conclusions】The incidence of BPE with PC in BPE patients undergoing checkups is higher. In addition to age, inhomogeneous echo of the prostate and urine pH are related factors for BPE with PC in BPE patients undergoing physical examinations.

Key words: benign prostatic enlargement; prostate calcification; healthy physical examinations; related factors

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良性前列腺增大(benign prostatic enlargement, BPE)通常用于描述40岁以上男性的良性前列腺增生(benign prostatic hyperplasia, BPH),伴有下尿路症状(lower urinary tract symptoms, LUTS)时为良性前列腺梗阻(benign prostatic obstruction, BPO)^[1-2]。前列腺体积(prostate volume, PV) ≥ 20 mL为前列腺增大的临界值,一些40岁以下的慢性前列腺炎(chronic prostatitis, CP)患者中也发现了前列腺增大^[3],故术语“BPE”理论上应包括BPH或CP引起的前列腺增大。前列腺钙化(prostate calcification, PC)影响BPE(继发于BPH或CP)引起的LUTS的表现及疗效^[4-5]。从组织学BPH到BPE,再到出现LUTS有一过程,约一半BPE者会发生LUTS^[6]。组织学BPH早期难于发现,CP诊断主要依据LUTS和侵入性前列腺按摩液检查。随着超声技术和体检的普及,BPE较早被发现,一些尚未发生LUTS的BPE者被观察到也伴有PC。进一步了解BPE伴PC的相关因素,有益于延缓LUTS的发生和改善其疗效。目前大样本研究BPE伴PC相关因素的报道较少,本研究回顾性分析了大样本男性的初次体检资料,分析了BPE伴PC的相关因素,现报道如下。

1 材料与方法

1.1 临床资料

按照入选和排除标准,2018年10月至2021年6月3 433名在安徽医科大学第四附属医院健康管理中心初次体检的男性资料被纳入分析,受试者年龄18~89岁。医院伦理委员会批准了本回顾性研

究(编号:PJ-YX2021-020)和豁免了受试者知情同意。入选标准:①18岁及以上男性;②完整的血、尿检测数据;③有腹部和泌尿系包括前列腺的超声检查结果。排除标准:①体检项目缺失者(包括泌尿系+前列腺超声检查);②总前列腺特异性抗原(total prostate specific antigen, TPSA) >10 $\mu\text{g/L}$ 和TPSA 4~10 $\mu\text{g/L}$ 并PSA比值 <0.16 者;③其它肿瘤标志物异常升高者;④影像检查示前列腺异常结节者;⑤恶性肿瘤者;⑥长期服用可能影响血脂等药物者,以避免影响代谢综合征(metabolic syndrome, MS)的评判;⑦估算肾小球滤过率(estimated glomerular filtration rate, eGFR) <60 mL/(min $\cdot 1.73$ m²)者,可能干扰血生化代谢物的水平;⑧可能影响PV的性腺轴器官疾病和性激素、5- α 还原酶抑制剂等药物服用者;⑨有任何前列腺手术者。

1.2 资料采集

体检者的人口学特征、既往史、药物使用史等由本中心已培训的专业人员采集,身高、体质量、体质指数(body mass index, BMI)、血压由专人负责测量和记录,采集晨10 mL尿液和空腹20 mL静脉血进行尿液、血液项目检测。纳入分析的受试者均行胸部CT或胸片检查及由超声科医生完成泌尿生殖系(含前列腺)、腹部脏器的经腹超声(transabdominal ultrasound, TAUS)检查,以符合排除标准。

1.3 血、尿液指标和PV等检测

血液指标包括血常规、血生化、血PSA、甲胎蛋白和癌胚抗原等肿瘤标志物的检测。尿液行尿常规检测。PV=(前列腺横径 \times 纵径 \times 前后径 $\times 0.52$) mL^[7]。有研究证实TAUS测量的PV <30 mL或横

断面成像时与经直肠超声测量的结果相当^[8]。

1.4 指标定义和诊断标准

MS诊断标准^[9]:①高血压:血压 $\geq 130/85$ mmHg和/或已确诊为高血压并治疗者。②高血糖:空腹血糖 ≥ 6.1 mmol/L,糖负荷后2 h血糖 ≥ 7.8 mmol/L和/或已确诊为糖尿病并治疗者。③空腹甘油三酯(triglyceride, TG) ≥ 1.70 mmol/L。④空腹高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDLc) < 1.04 mmol/L。⑤肥胖: BMI ≥ 28 kg/m²或腹型肥胖腰围男性 ≥ 90 cm; BMI ≥ 25 kg/m²为超重。MS为有以上3项或更多项者。诊断BPE的PV尚无统一的标准,根据之前的文献报告^[1-2],建议使用20 mL。本研究BPE定义为符合排除标准的无BPH组织学证实下的PV ≥ 20 mL者。PC为前列腺内离散、小强回声或大量多发粗糙强回声灶,伴或不伴后方声影^[10]。前列腺回声不均均为前列腺实质内紊乱的不均匀回声光点,低回声区伴高回声^[11]。

1.5 统计学方法

数据使用SPSS 22.0统计软件处理,以均数 \pm 标准差 $\bar{x} \pm s$ 表示服从正态分布的计量资料,两组比较使用 t 检验;以中位数和四分位间距 $M(IQR)$ 表示非正态分布计量资料,两组比较使用Mann-Whitney U 检验。以率或构成比(%)表示计数资料,使用 χ^2 检验。使用Logistic回归模型进行多因素影响因素分析。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 体检男性BPE伴PC发生率及一般情况

3 433名体检男性中BPE 863例,年龄20~89岁。BPE伴PC在BPE者中的发生率为37.5% (324/863)。A组(BPE伴PC)年龄27~89岁,中位52岁。B组(BPE不伴PC)年龄20~86岁,中位49岁(表1)。BPE者各年龄段BPE伴PC发生率差异有统计学意义($P < 0.05$),随年龄增加呈增加走势(趋势 $\chi^2 = 22.201, P = 0.000$;表2)。

2.2 A组与B组指标比较

A组年龄、血尿素氮、尿PH值高于B组($P < 0.05$),身高、体质量、淋巴细胞数、血尿酸、eGFR低于B组($P < 0.05$;表1)。A组前列腺回声不均患者

比例高于B组($P < 0.05$)。两组间MS及各组分患者比例差异无统计学意义($P > 0.05$;表2)。

2.3 体检男性BPE者BPE伴PC的相关因素分析

依据单因素分析结果,以年龄、血尿酸、前列腺回声不均等为自变量,BPE伴PC为因变量。分类变量的具体赋值见表3下面的注解,年龄分类变量设置哑变量。Logistic回归分析(逐步向前法)显示前列腺回声不均、尿PH值和年龄是体检BPE者BPE伴PC的独立相关因素(表3)。

3 讨论

近年来研究发现BPO、CP和前列腺癌常伴发PC^[12-13]。PC不仅影响BPO等良性前列腺疾病的症状还影响这些疾病的疗效^[14]。BPO有BPE和LUTS,但有BPE并不一定意味着BPO。BPO与PC的关系及联系机制目前仍不清楚。泌尿、男科医生诊治的大部分BPO是无组织学证据的,是通过影像学上的BPE、LUTS结合血PSA等检查获得诊断和治疗的。随着体检的普及,观察到部分BPE在未发展到有LUTS的BPO时已伴发PC,BPE伴PC也出现在青年男性中,具体病因不清。BPE伴PC在BPE者中的发生率及相关因素研究报道少见。本研究基于大样本成年男性的初次体检数据,对BPE伴PC在BPE者中的发生率及相关因素进行了单因素和多因素的分析,结果显示863例BPE中合并PC 324例,BPE者BPE伴PC发生率为37.5%。BPE者中BPE伴PC不仅出现在青年中,且随年龄增长发生比例也增加。前列腺回声不均、尿PH值和年龄是BPE者BPE伴PC的相关因素。年龄因素与其他学者报道的PC影响因素结果相同。

BPE伴PC在BPE中发生率的研究报道少见,而PC在BPO或BPH者中的发生率及影响作用有一些报道。Han等^[4]对539例BPO研究发现合并PC 188例,患病率34.9%,PC与尿路症状严重程度独立相关。Kuei等^[14]报道112例BPO中PC发病率为42.9%(48/112),BPO伴PC患者的预后改善率(47.9%)明显低于BPO不伴PC患者(71.9%)。Logistic回归分析显示,在调整年龄、PV后,PC是不良医疗结果的预测因子。Meng等^[15]研究了4 738例

表1 两组患者指标特征的比较

Table 1 Comparison of indexes characteristics between the group A and group B [M (IQR) or ($\bar{x} \pm s$)]

Characteristics	Group A ($n=324$)	Group B ($n=539$)	z/t	P
Age/years	52.00(14.00)	49.00(17.00)	-4.577	0.000
Height/cm	170.00(7.50)	171.00(8.00)	-2.766	0.006
Weight/kg	72.70(12.18)	73.90(12.30)	-2.039	0.041
Body mass index/(kg/m^2)	25.11(3.41)	25.13(3.83)	-0.757	0.449
SBP/mmHg	134.00(23.00)	134.00(27.00)	-0.664	0.507
DBP/mmHg	84.00(14.00)	85.00(16.00)	-1.065	0.287
Lymphocyte count/ $(\times 10^9/\text{L})$	1.86(0.70)	1.96(0.69)	-2.226	0.026
Hemoglobin/(g/L)	152.00(13.00)	153.00(13.00)	-1.058	0.290
Serum total protein/(g/L)	71.02 \pm 4.80	71.40 \pm 4.45	-1.154	0.249
Blood urea nitrogen/(mmol/L)	5.46(1.73)	5.27(1.68)	-2.102	0.036
Serum creatinine/ $(\mu\text{mol}/\text{L})$	70.30(14.70)	70.40(14.60)	-0.166	0.868
Serum uric acid/ $(\mu\text{mol}/\text{L})$	353.50(105.25)	367.00(103.00)	-2.199	0.028
eGFR/[$\text{mL}/(\text{min}\cdot 1.73\text{ m}^2)$]	110.43(42.64)	120.46(38.62)	-3.816	0.000
Fasting blood glucose/(mmol/L)	5.07(0.90)	5.03(0.77)	-1.739	0.082
Serum TG/(mmol/L)	1.41(0.99)	1.42(1.01)	-0.303	0.762
Serum HDLc/(mmol/L)	1.13(0.38)	1.14(0.37)	-0.386	0.700
Serum LDLc/(mmol/L)	2.91(1.01)	2.79(0.98)	-1.333	0.183
Serum TC/(mmol/L)	4.75(1.00)	4.75(1.12)	-0.176	0.860
PV/mL	25.83(7.54)	25.43(7.23)	-1.145	0.252
Serum TPSA/ $(\mu\text{g}/\text{L})$	1.15(1.08)	1.11(0.89)	-1.912	0.056
Urine pH	6.31 \pm 0.70	6.16 \pm 0.70	2.917	0.004
Urine specific gravity	1.020 \pm 0.007	1.021 \pm 0.007	-1.320	0.187

SBP: systolic blood pressure; DBP: diastolic blood pressure; BPE: benign prostatic enlargement; PC: prostate calcification; eGFR: estimated glomerular filtration rate; TG: triglyceride; HDLc: high-density lipoprotein cholesterol; LDLc: low-density lipoprotein cholesterol; TC: total cholesterol; PV: prostate volume; TPSA: total prostate-specific antigen.

BPH,发现伴发PC 3 630例,患病率为76.61%,但文中没有提供诊断BPH的组织学证据和PV标准,也没有提供LUTS数据。

BPE者BPE伴PC的相关因素研究尚未见报道,但PC影响因素的研究有少许报道。Tang等^[16]对13 869名PC者研究发现年龄、前列腺前后径、TG和HDLc水平是PC的危险因素。Balasar等^[17]报道PC的存在率在血尿酸 $>0.07\text{ g}/\text{L}$ 组30.49% (25/82)显著高于尿酸 $<0.07\text{ g}/\text{L}$ 组14.94% (13/87) ($P=0.015$),多因素分析显示尿酸 $>0.07\text{ g}/\text{L}$ 组发生PC的几率是尿酸 $<0.07\text{ g}/\text{L}$ 组的2.89倍($P=0.013$)。Meng等^[15]分析了14 427名男性中PC的影响因素,

显示年龄、BMI、尿酸、BPH和前列腺囊肿是PC的独立影响因素,但文中未排除TPSA $>10\mu\text{g}/\text{L}$ 前列腺癌疑似者。上述文献报道的是PC影响因素的研究,有关BPE者BPE伴PC的相关因素研究尚未见报道。本研究筛除前列腺恶性肿瘤疑似者,样本量较大,基本涵盖成人全年龄段。

PC发生的具体机制尚不清楚,目前与以下机制有关:一是前列腺腺管不畅,前列腺分泌物中物质沉淀,淀粉酶体在炎症作用下形成钙化;二是尿液反流入前列腺内促进钙化物形成^[12];三是微生物生物膜在PC发生中也有一定的作用,有研究报道PC核心部位的活检标本分离出大肠杆菌、粪肠球

表2 BPE者各年龄段BPE伴PC发生率及各指标下(除年龄)两组患者比例比较
Table 2 Incidence of BPE with PC in the BPE group in different ages and comparison of the proportion of patients under different indexes (excluding age) between group A and group B [n(%)]

Variables		Group A (n=324)	Group B (n=539)	χ^2	P
Age/years	20~29	4(10.8)	33(89.2)	29.370	0.000
	30~39	46(29.7)	109(70.3)		
	40~49	87(39.4)	134(60.6)		
	50~59	103(37.1)	175(62.9)		
	60~69	48(44.0)	61(56.0)		
	70~79	28(53.8)	24(46.2)		
	80~89	8(72.7)	3(27.3)		
Hyperglycemia/(mmol/L)	Yes (≥ 6.1)	43(13.3)	65(12.1)	0.272	0.602
	No (< 6.1)	281(86.7)	474(87.9)		
High triglyceride/(mmol/L)	Yes (≥ 1.7)	117(36.1)	190(35.3)	0.065	0.798
	No (< 1.7)	207(63.9)	349(64.7)		
Low HDLc/(mmol/L)	Yes (< 1.04)	123(38.0)	179(33.2)	2.010	0.156
	No (≥ 1.04)	201(62.0)	360(66.8)		
Overweight/(kg/m ²)	Yes (BMI ≥ 25)	170(52.5)	281(52.1)	0.009	0.924
	No (BMI < 25)	154(47.5)	258(47.9)		
Obesity/(kg/m ²)	Yes (BMI ≥ 28)	53(16.4)	98(18.2)	0.466	0.495
	No (BMI < 28)	271(83.6)	441(81.8)		
Hypertension/mmHg	Yes (BP $\geq 130/85$)	231(71.3)	353(65.5)	3.117	0.077
	No (BP $< 130/85$)	93(28.7)	186(34.5)		
MS	Yes	68(21.0)	107(19.9)	0.162	0.688
	No	256(79.0)	432(80.1)		
Inhomogeneous echo of the prostate	Yes	24(7.4)	22(4.1)	4.436	0.035
	No	300(92.6)	517(95.9)		

BPE: benign prostatic enlargement; PC: prostate calcification; TG: triglyceride; HDLc: high-density lipoprotein cholesterol; BMI: body mass index; MS: metabolic syndrome.

菌等^[18]。本结果显示除年龄外,前列腺回声不均和尿PH值也是BPE者BPE伴PC的独立相关因素。在良性前列腺病变中,超声发现前列腺不均回声通常表明前列腺局部存在炎症^[11],这可能促进淀粉酶体和其他组织的钙化;尿PH值可能与高PH值尿液反流入前列腺内易促进钙化的形成。依据化学特性,钙盐沉淀在高PH环境中容易发生,有报道高碱性尿液可导致急性膀胱炎和前列腺炎^[19-20]。年龄增长伴随的器官组织钙化可能与衰老有关。BPE本身可能是PC的影响因素,与BPE导致前列腺腺管不畅有关,但本结果PV不是BPE伴PC的相关

因素。

本研究局限于单中心体检人群的资料,这可能对男性群体的选择偏差,但大量的3 433个样本可能是减少偏差的一种方法;其次,未评估BPE伴PC对BPE者临床症状和性生活的影响及BPO和CP患者的数量;再者,前列腺超声检查非一位超声医生完成,可能存在操作者间的诊断差异,但技术娴熟的超声医生可降低此类偏差。因此,结果解释需谨慎,需要更大样本量的多中心研究来进一步验证结果。

总之,本研究结果显示体检BPE者BPE伴PC

表3 BPE者BPE伴PC的相关因素多因素回归分析(逐步向前法)
Table 3 Multivariate logistic regression analysis of BPE with PC related factors in BPE patients receiving physical examinations

Variables	<i>b</i>	<i>S_b</i>	Wald χ^2	<i>P</i>	\hat{OR}	OR 95%CI
Constant	-4.263	0.874	23.814	0.000	0.014	
inhomogeneous echo of the prostate	0.741	0.323	5.254	0.022	2.099	(1.113, 3.955)
Urine pH value	0.344	0.107	10.229	0.001	1.410	(1.142, 1.740)
Age/years			25.084	0.000		
30~39	1.174	0.562	4.361	0.037	3.235	(1.075, 9.737)
40~49	1.605	0.551	8.468	0.004	4.976	(1.688, 14.664)
50~59	1.547	0.548	7.957	0.005	4.695	(1.603, 13.571)
60~69	1.918	0.569	11.350	0.001	6.808	(2.230, 20.778)
70~79	2.217	0.607	13.349	0.000	9.176	(2.794, 30.134)
80~89	2.881	0.873	10.900	0.001	17.829	(3.224, 98.594)

OR: odds ratio; CI: confidence interval. Classification variable assignment: dependent variable: 1=BPE with PC, 0=BPE without PC; Independent variables: 1=Hypertension, 0=non-hypertension; 1=inhomogeneous echo of the prostate, 0=non-inhomogeneous echo of the prostate. The age groups categorical variables were set as dummy variables, where 0=20~29 years old group.

的发生率较高,随年龄增加而增加。除年龄外,前列腺回声不均和尿PH值也是体检BPE者BPE伴PC的独立相关因素。年龄无法改变,但可以主动

改变尿PH值和前列腺回声不均来控制BPE伴发PC,可能有利于BPE伴PC的防治,进而有益于BPE导致的LUTS的防治。

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