doi: 10.13241/j.cnki.pmb.2015.01.016

# 血糖与前列腺癌患者的关系 *

唐 敬[1] 李 纲[1△] 殷虎明[1] 沈卫东[2] 张学锋[1] 浦金贤[1] 侯建全[1]

（1 苏州大学附属第一医院泌尿外科 江苏 苏州 215006；2 苏州大学附属第一医院超声科 江苏 苏州 215006）

**摘要 目的：**探讨前列腺活检患者的血糖与前列腺癌患者的关系。**方法：**前瞻性收集 416 例初次经直肠超声引导下前列腺穿刺活检患者的血糖、前列腺特异性抗原（PSA）和 Gleason 评分等临床资料，所有患者以血糖浓度 6.1 mmol/L 为界分成两组，比较高血糖组和正常血糖组前列腺癌检出率和 Gleason 评分的差异。**结果：**416 例前列腺活检患者中，检出前列腺癌 165 例，高血糖组 38 例（40.00%），正常血糖组 127 例（39.56%），差异无统计学意义（P>0.05）；低级别前列腺癌（Gleason<7 分）患者的构成比分别为 0.184、0.071，差异有统计学意义（P<0.05），Spearman 等级相关分析显示前列腺癌患者的血糖值与 Gleason 评分呈负相关（r=-0.228，P<0.05）。**结论：**血糖对前列腺活检患者中前列腺癌检出率没有影响，但提高了低级别前列腺癌患者的构成比，血糖是影响前列腺癌 Gleason 评分的一个独立因素。

**关键词：**前列腺活检；前列腺癌；前列腺增生；血糖

**中图分类号：**R737.25 **文献标识码：**A **文章编号：**1673-6273（2015）01-69-03

# The Relationship between Blood Glucose and Prostate Cancer Patients*

*TANG Jing[1], LI Gang[1△], YIN Hu-ming[1], SHEN Wei-dong[2], ZHANG Xue-feng[1], PU Jin-xian[1], HOU Jian-quan[1]*

*(1 Department of Urology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, 215006, China;*

*2 Department of Ultrasound, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, 215006, China)*

**ABSTRACT Objective:** To discuss the relationship between blood glucose of prostate biopsy patients and prostate cancer patients. **Methods:** We prospectively collected the blood glucose, prostate specific antigen, Gleason score and other clinical data of 416 patients who underwent prostate biopsy guided by transrectal ultrasound (TRUS) first time. All patients were divided into two groups by the concentration of 6.1 mmol/L of blood glucose, and the differences of the detection rate of prostate cancer and Gleason score were compared between the hyperglycemia and the normal blood glucose groups. **Results:** There were 165 cases of prostate cancer was detected in 416 patients with prostate biopsy, including 38 cases (40.00%) and 127 cases (39.56%) in the hyperglycemia and the normal blood glucose groups, respectively, it was no statistically significant difference (P > 0.05). However, the constituent ratio of low grade prostate cancer (Gleason<7) was 0.184, 0.071, respectively, the difference was statistically significant (P<0.05). Spearman rank correlation analysis showed that the levels of blood glucose in prostate cancer patients negatively correlated with Gleason score (r=-0.228, P<0.05). **Conclusions:** The blood glucose had no statistically significant effect on the detection rate of prostate cancer in patients with prostate biopsy, but raising the constituent ratio of low grade prostate cancer (Gleason<7). Blood glucose might be used as an independent factor influencing on Gleason score of prostate cancer in patients with prostate biopsy.

**Key words:** Prostate biopsy; Prostate cancer; Benign prostatic hyperplasia; Blood glucose

**Chinese Library Classification (CLC): R737.25 Document code: A**

**Article ID: 1673-6273(2015)01-69-03**

## 前言

流行病学研究表明，糖尿病与前列腺癌的风险相关，但这一风险尚存在争议。美国在一项为期 16 年的以 51529 名卫生工作者为对象的随访研究中发现糖尿病患者患前列腺癌的风险明显低于非糖尿病患者（HR：0.83，95%CI：0.74-0.94）[1]，Rosenberg 等在以医院为基础的病例对照研究中同样发现糖尿病患者发生前列腺癌的风险较低[2]，英国一项 55215 例 PSA 筛查的病例对照研究显示糖尿病降低前列腺癌的风险（OR：0.78，95%CI：0.61-0.99）[3]，这些研究说明血糖对前列腺癌可能存在保护作用，但这种保护作用在日本的一项研究中没有得到证实[4]，Kang[5]和 Fukushima[6]在研究糖尿病与前列腺癌的风险和分级时发现糖尿病增加前列腺癌的风险。上述研究涉及糖尿病与前列腺癌的风险相关，但结论不一致，而血糖与前列腺癌之间的关系仍不清楚，本文对我院 416 例前列腺穿刺活检患者的血糖结果进行前瞻分析，探讨血糖对前列腺癌检出率和 Gleason 评分的影响。

* 基金项目：江苏省医学重点人才资助项目（RC2011108）；江苏省医学重点学科建设项目（XK201151）

作者简介：唐敬（1986-），男，硕士研究生，主要研究方向：前列腺癌的基础与临床，电话：18862332481，E-mail：20115232043@suda.edu.cn

△通讯作者：李纲，教授，医学博士，E-mail:gangli@suda.edu.cn

（收稿日期：2014-07-12 接受日期：2014-08-07）

## 1 资料与方法

### 1.1 临床资料

2010 年 2 月～2013 年 2 月入住我科的 416 例前列腺穿刺活检患者，年龄 52～87 岁，平均 69.62 岁；PSA0.27～642.00 ng/mL，中位数 16.54 (9.64～41.25) ng/mL；体重指数（BMI）12.40～33.98 kg/m$^2$，中位数 24.22（21.95～25.78）kg/m$^2$；前列腺体积（TPV）10.02～297.16 mL，中位数 39.61 (28.37～64.09) mL；血糖 3.8～20.48 mmol/L，中位数 5.40(5.02～5.99) mmol/L。

### 1.2 方法

**1.2.1 血糖值的来源** 所有患者以穿刺前一天的空腹血糖值作为本次血糖值，将空腹血糖高于正常高限 6.1 mmol/L 定义为高血糖。为了排除饮食、药物等因素对本研究的影响，把血糖正常但有糖尿病病史的患者划分在高血糖组。

**1.2.2 经直肠超声穿刺活检** 采用配有 8-MHz 经直肠探头的西门子 Sequoia-512 型彩色多普勒超声诊断仪。穿刺时，患者取左侧卧位，臀部朝向术者并尽量靠近床边，常规穿刺 12 针，对重点可疑区域加穿 1-2 针，前列腺组织标本用 10%中性福尔马林固定送病理检查。通过公式：体积 =0.52* 前后径 * 上下径 * 横径，计算出前列腺总体积（TPV）。

### 1.3 统计学处理

采用 SPSS17.0 统计软件分析数据。正态分布资料用均数± 标准差（$\bar{x}\pm s$）表示，偏态分布资料用中位数（P50）及四分位数间距（P25-P75）表示，血糖与 Gleason 评分及前列腺活检患者临床参数等指标的关系用 Spearman 相关性分析进行检验，两组具有正态性及方差齐性的资料比较用 t 检验，非正态性及方差齐性的资料比较用秩和检验，计数资料用 $x^2$ 检验，$P<0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 前列腺癌（PCa）和前列腺增生（BPH）患者的血糖等临床资料

416 例前列腺穿刺活检患者的血糖中位数及四分位数间距分别为 5.40 mmol/L 和 5.02～5.99 mmol/L，其中前列腺癌患者为 5.49 mmol/L 和 5.05～6.13 mmol/L，前列腺增生患者为 5.39 mmol/L 和 5.01～5.96 mmol/L，两者之间差异无统计学意义（P>0.05）。而与前列腺癌及前列腺增生疾病有关的年龄、前列腺特异性抗原（PSA）、体重指数（BMI）、前列腺总体积（TPV）等指标，两者之间差异均有统计学意义（P<0.05）（表 1）。

**表 1 前列腺癌和前列腺增生患者的临床资料**

Table 1 Clinical data of patients with prostate cancer and benign prostate hyperplasia

| Clinical parameters | PCa(n=165) | BPH(n=251) | | P-value |
|---|---|---|---|---|
| Age(years) | 72.09± 8.60[a] | 67.97± 8.48a | t = 4.686 | 0.000 |
| PSA(ng/ml) | 49.00(20.38～100.00)[b] | 10.92(6.87～18.86)[b] | z =-11.646 | 0.000 |
| BMI(kg/m$^2$) | 23.53(21.30～25.36)[b] | 24.45(22.49～25.78)[b] | z =-2.479 | 0.013 |
| TPV(cm$^3$) | 37.34(23.61～66.74)[b] | 42.88(31.49～61.89)[b] | z =-2.246 | 0.025 |
| Glucose(mmol/L) | 5.49(5.05～6.13)[b] | 5.39(5.01～5.96)[b] | z=-0.278 | 0.782 |

Note: a: $\bar{x}\pm s$ b: $P_{50}$ ($P_{25}$-$P_{75}$).

### 2.2 高血糖组和正常血糖组中前列腺癌检出率及前列腺癌 Gleason 评分的比较

416 例前列腺穿刺活检患者中，检出前列腺癌 165 例，其中高血糖组 38 例（40.00%），正常血糖组 127 例（39.56%），两组之间检出率差异无统计学意义（$x^2$=0.006, P=0.939）。高血糖组前列腺癌患者中低级别前列腺癌（Gleason＜7 分）的构成比为 0.184，明显高于正常血糖组的 0.071，差异有统计学意义（$x^2$=4.291, P=0.038）（表 2）。

**表 2 高血糖组和正常血糖组中前列腺癌检出率及前列腺癌 Gleason 评分的比较**

Table 2 Comparison of the detection rate and gleason score of prostate cancer between the hyperglycemia group and the normal blood glucose group

| | Glucose＜6.1mmol/L | Glucose≥ 6.1mmol/L | | P-value |
|---|---|---|---|---|
| Biopsy results | | | $x^2$=0.006 | 0.939 |
| PCa | 127 | 38 | | |
| BPH | 194 | 57 | | |
| Gleason score | | | $x^2$= 4.291 | 0.038 |
| ＜7 | 9 | 7 | | |
| ≥ 7 | 118 | 31 | | |

### 2.3 血糖与前列腺癌 Gleason 评分等临床参数的相关分析

Spearman 相关分析显示血糖与前列腺癌患者 Gleason 评分呈负相关（r=-0.228，P<0.05），与 BMI 呈正相关（r=0.267，P<0.05），而与年龄、TPV、PSA 等指标无相关性（P>0.05）。

表 3 血糖与前列腺癌 Gleason 评分等临床参数的相关分析

Table 3 The correlation analysis of the blood glucose and gleason score of prostate cancer and other clinical parameters

| | Glucose | |
|---|---|---|
| | r | P-value |
| Age(years) | -0.059 | 0.214 |
| BMI(kg/m$^2$) | 0.267 | 0.000 |
| TPV(cm$^3$) | 0.088 | 0.138 |
| PSA(ng/ml) | 0.059 | 0.212 |
| Gleason(score) | -0.228 | 0.042 |

## 3 讨论

前列腺癌是老年男性常见疾病。随着我国人口的老龄化和生活习惯的改变,前列腺癌的发病率呈明显上升趋势,且越来越年轻化。国外的研究显示,糖尿病与结直肠癌、乳腺癌、子宫内膜癌等肿瘤发病升高有关,而糖尿病与前列腺癌之间的关系各家研究不一致,与国外相比[7-9],我国有关糖尿病与前列腺癌之间的研究较少,而前列腺穿刺活检患者的血糖与前列腺癌关系的研究更是一片空白。

影响前列腺癌检出率的因素有很多, 如年龄、PSA、BMI、TPV等。谢立平等人经统计分析发现年龄与前列腺癌检出率成正相关[10],Aganovic[11]和 Jeon[12]等发现 TPV、BMI 与前列腺癌检出率成负相关, Lodeta[13]和 Jeon[12]等报道 PSA 水平与前列腺癌检出率成正相关,这些结论与我们的研究相一致。

依据 PSA、Gleason 评分及临床分期(TNM)三个指标将前列腺癌划分为低危、中危、高危三组[14],这对决定患者的治疗方案和判断预后是极其重要的。本资料显示,血糖对前列腺癌检出率没有明显影响, 但提高了低级别前列腺癌患者的构成比,与高级别前列腺癌患者相比,此类患者预后相对较好,这显示血糖对前列腺癌患者的潜在保护作用是通过影响 Gleason 评分来实现的。

糖尿病降低前列腺癌风险的研究报道很多,但血糖对其保护机制尚未阐明。前列腺癌大部分为雄激素依赖性,在其生长和进展方面,雄激素受体扮演者重要的作用[15]。Barbosa 等人[16]证实增加血糖浓度可以下调雄激素受体 (AR)mRNA 水平,在体内试验表明,链脲霉素诱导的糖尿病使肿瘤生长迟缓,雄激素受体在 PAC120 前列腺癌小鼠中的表达也显著减少,证明了高血糖通过下调雄激素受体水平来降低前列腺癌的风险。

前列腺癌的发生与基因和环境等多种因素有关,其中遗传因素占到 42%[15]。最近的基因研究都表明Ⅱ型糖尿病和前列腺癌的风险有关[17,18],考虑到单核苷酸多态性(SNP)可以影响前列腺癌的风险,Piercel 等[19]在一个大型的前列腺癌病例对照研究中发现Ⅱ型糖尿病的风险等位基因数与前列腺癌呈负相关,和最低组相比(<17 个风险等位基因),最高四分位数组(> 20 个风险等位基因)的Ⅱ型糖尿病等位基因数降低前列腺癌的风险(OR=0.77,95%CI:0.60-0.99),说明Ⅱ型糖尿病的遗传易感性增加可以降低前列腺癌的风险。但这项研究并未涉及血糖,遗传易感性可能和血糖高低有着潜在的联系,因此未来的研究应结合血糖和遗传易感性来综合分析。

总之,在前列腺穿刺活检患者中,血糖对前列腺癌检出率没有明显影响,但影响了前列腺癌 Gleason 评分,对前列腺癌患者具有潜在的保护作用,这种潜在保护作用的机制可能是高血糖提高了低级别前列腺癌患者的构成比,这一结论尚有待进一步扩大样本进行研究和证实。

### 参 考 文 献(References)


[1] Kasper JS, Liu Y, Giovannucci E. Diabetes mellitus and risk of prostate cancer in the health professionals follow-up study [J]. Int J Cancer, 2009, 124(6): 1398-1403

[2] Rosenberg DJ, Neugut AI, Ahsan H, et al. Diabetes mellitus and the risk of prostate cancer[J]. Cancer Invest, 2002, 20(2): 157-165

[3] Turner EL, Lane JA, Donovan JL, et al. Association of diabetes mellitus with prostate cancer: nested case-control study (Prostate testing for cancer and treatment study) [J]. Int J Cancer, 2011, 128 (2): 440-446

[4] Li Q, Kuriyama S, Kakizaki M, et al. History of diabetes mellitus and the risk of prostate cancer: the Ohsaki Cohort Study[J]. Cancer Causes Control, 2010, 21(7): 1025-1032

[5] Kang J, Chen MH, Zhang Y, et al. Type of diabetes mellitus and the odds of Gleason score 8 to 10 prostate cancer [J]. Int J Radiat Oncol Biol Phys, 2012, 82(3): e463-467

[6] Fukushima H, Masuda H, Kawakami S, et al. Effect of diabetes mellitus on high-grade prostate cancer detection among Japanese obese patients with prostate-specific antigen less than 10 ng/mL [J]. Urology, 2012, 79(6): 1329-1334

[7] Werny DM, Saraiya M, Gregg EW. Prostate-specific antigen values in diabetic and nondiabetic US men, 2001-2001 [J]. Am J Epidemiol, 2006, 164(10): 978-983

[8] Hong SK, Oh JJ, Byun SS, et al. Impact of diabetes mellitus on the detection of prostate cancer via contemporary multi(≥ 12)-core prostate biopsy[J]. Prostate, 2012, 72(1): 51-57

[9] Zhang W, Hu R. Why does diabetes offer protective effects a gainst prostate cancer? The possible role of its microvascular complications [J]. Med Hypotheses, 2010, 74(2): 242-243

[10] 谢立平, 秦杰, 郑祥毅, 等. 481 例前列腺癌患者年龄与病理构成分析[J]. 中华男科学杂志, 2005, 11(6): 28-30
Xie Li-ping, Qin Jie, Zheng Xiang-yi, et al. The age and pathological analysis of 481 prostate cancer patients[J]. Chinese Journal of Andrology, 2005, 11(6): 28-30

[11] Aganovic D, Prcic A, Kulovac B, et al. Influence of the prostate volume, prostate specific antigen density and number of biopsy samples on prostate cancer detection[J]. Med Arh, 2012, 66(1): 41-44


(下转第 83 页)

的选择。

## 参 考 文 献(References)


[1] Trottier H, Burchell AN. Epidemiology of mucosal human papillomavirus infection and associated diseases[J]. Public Health Genomics, 2009, 12(5-6): 291-307

[2] 米贤军, 白宝敏, 刘勇, 等. Thinprep 液基细胞学检查在子宫颈病变中的应用研究 [J]. 中国医师杂志, 2005, 7(4) : 493-495
Mi Xian-jun, Bai Bao-min, Liu Yong, et al. Application Study of Thinprep Liquid Based Cytology Test in the Detection of Cervical Diseases [J]. Journal of Chinese Physician, 2005, 7(4): 493-495

[3] Haverkos HW. Multifactorial etiology of cervical cancer: a hypothesis [J]. MedGenMed , 2005, 7(4): 57

[4] Henero R, Hildesheim A, Bratti C, et al. Population-based study of human papillomavirus infection and cervical neoplasia in rural costa Rica [J]. J Natl Cancer Inst, 2000, 92(6): 464-474

[5] Dahlström LA, Ylitalo N, Sundström K, et al. Prospective study of human papillomavirus and risk of cervical adenocarcinoma [J]. Int J Cancer, 2010, 127(8): 1923-1930

[6] 黄晓晴, 李跃红, 王华峰. 探讨宫颈糜烂与宫颈上皮内瘤变的关系 [J].中国现代医生, 2011, 49(5): 34-35
Huang Xiao-qing, Li Yue-hong, Wang Hua-feng. Discussion on the Relationship between Cervical Erosion and Cervical InTraepithelial Neoplasia [J]. China Modern Doctor, 2011, 49(5): 34-35

[7] 姜桂芳. 3008 例已婚妇女宫颈癌筛查结果分析 [J]. 吉林医学, 2012, 33(22): 4812-4813
Jiang Gui-fang. Analysis of the results of 3008 cases of married women in cervical cancer screening [J]. Jilin Medical Journal, 2012, 33(22): 4812-4813

[8] Okonkwo C, Ezeanochie M, Olagbuji B. Physical after effects and clients satisfaction following colposcopy and cervical biopsy in a Nigerian population [J]. Afr Health Sci, 2013, 13(2): 402-406

[9] Stormo AR, Espey D, Glenn J, et al. Findings and lessons learned from a multi-partner collaboration to increase cervical cancer prevention efforts in Bolivia [J]. Rural Remote Health, 2013, 13(4): 2595

[10] Suh DH, Kim JW, Aziz MF, et al. Asian society of Gynecologic Oncology Workshop 2010 [J]. J Gynecol Oncol, 2010, 21(3): 137-150

[11] McAdam M, Sakita J, Tarivonda L, et al. Evaluation of a cervical cancer screening program based on HPV testing and LLETZ excision in a low resource setting [J]. PLoS ONE, 2010, 5(10): e13266

[12] 王临红, 邱秀, 郑睿敏, 等. 我国宫颈癌流行病学状况及防治策略的回顾与展望[J]. 中国妇幼卫生杂志, 2010, 1(3): 145-149
Wang Lin-hong, Qiu Xiu, Zhang Rui-min, et al. Review and prospection of epidemiology and preventive and treatment strategy of cervix cancer in china [J]. Chin J Women Child Health, 2010, 1(3): 145-149

[13] Grce M. Primary and secondary prevention of cervical cancer [J]. Exp Rev Mol Diagn, 2009, 9(8): 851-857

[14] 孟瑞琳, 马文军, 许燕君, 等. 广东省妇女乳腺癌和宫颈癌筛查率及相关影响因素分析[J] . 华南预防医学, 2010, 36(2): 8-10,14
Meng Rui-lin, Ma Wen-jun, Xu Yan-jun, et al. The analysis of relative factors of the rate of women breast and cervix cancer screening in Guangdong province, south China [J]. J Prevent Med, 2010, 36(2): 8-10,14

[15] Lippman SA, Sucupira MC, Jones HE, et al. Prevalence, distribution and correlates of endocervical human papillomavirus types in Brazilian women [J]. Int J STD AIDS, 2010, 21(2): 105-109

[16] Insinga RP, Liaw KW, Johnson LG, et al. A systematic review of the prevalence and attribution of human papillomavirus types among cervival, vaginal and vulvar precancers and cancers in the United States [J]. Cancer Epidemiol Biomarkers Prev, 2008, 17(7): 1611-1622

[17] Siebers AG, Klinkhamer PM, Grefte JM, et al. Comparison of liquid-based cytology with conventional cytology for detection of cervical cancer precursors [J]. JAMA, 2009, 302(16): 1757-1764

[18] Sankaranarayanan R, Budukh AM, Rajkumar R. Effective screening programmes for cervical cancer in low and middle income developing countries [J]. Bull World Health Organ, 2001, 79(10): 954-962

[19] Grce M, Matovina M, Milutin-Gasperov N, et al. Advances in cervical cancer control and future perspectives [J]. Coll Antropol, 2010, 34(2): 731-736

[20] Hewson KA, Browning GF, Devlin JM, et al. Application of high-resolution melt curve analysis for classification of infectious bronchitis viruses in field specimens [J]. Aust Vet, 2010, 88(10): 408-413


(上接第 71 页)


[12] Jeon KP, Jeong TY, Lee SY, et al. Prostate cancer in patients with metabolic syndrome is associated with low grade Gleason score when diagnosed on biopsy[J]. Korean J Urol, 2012, 53(9): 593-597

[13] Lodeta B, Benko G, Trkulja V. Increasing prostate-specific antigen levels differently influence prostate cancer detection rates of two different 12-core prostate biopsy schemes [J]. Urol Int, 2013, 91 (1): 75-80

[14] 那彦群, 叶章群, 孙光, 等. 中国泌尿外科疾病诊断治疗指南[M]. 北京:人民卫生出版社, 2011: 49-79
Na Yan-qun, Ye Zhang-qun, Sun Guang, et al. The Chinese guidelines to diagnosis and treatment of urology disease[M]. Bei Jing: People's Medical Publishing House, 2011: 49-79

[15] Grossmann M, Wittert G Androgens. Diabetes and Prostate cancer[J]. Endocr Relat Cancer, 2012, 19(5): F47-62

[16] Barbosa-Desongles A, Hernández C, De Torres I, et al. Diabetes protects from prostate cancer by downregulating androgen receptor: new insights from LNCaP cells and PAC120 mouse model [J]. PLoS One, 2013, 8(9): e74179

[17] Frayling TM, Colhoun H, Florez JC. A genetic link between type 2 diabetes and prostate cancer [J]. Diabetologia, 2008, 51 (10): 1757-1760

[18] Yeager M, Orr N, Hayes RB, et al. Genome-wide association study of prostate cancer identifies a second risk locus at 8q24 [J]. Natural genetic, 2007, 39(5): 645-649

[19] Pierce BL, Ahsan H. Genetic susceptibility to type 2 diabetes is associated with reduced prostate cancer risk [J]. Hum Hered, 2010, 69(3): 193-201