

前列腺癌

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经直肠和经会阴前列腺穿刺对前列腺癌诊断价值的比较

王林峰,罗生军,唐伟

(重庆医科大学附属第一医院泌尿外科,重庆 400016)

【摘要】目的:比较超声引导下经直肠前列腺系统穿刺(transrectal prostate systematic biopsy,TR-SB)和磁共振-超声引导下经会阴前列腺融合靶向穿刺(transperineal prostate targeted biopsy,TP-TB)对前列腺癌(prostate cancer,PCa)检出率的差异,探讨两者的诊断价值。**方法:**回顾性地分析重庆医科大学附属第一医院2020年12月至2022年5月的行经直肠和经会阴前列腺穿刺活检术的患者共310例,按穿刺方式将患者分为TR-SB组和TP-TB组,比较2种穿刺方式对前列腺癌、临床有意义的前列腺癌(clinically significant prostate cancer,CSPCa)检出率和并发症的差异。**结果:**在总前列腺特异性抗体(total prostate specific antigen,tPSA)4~50 ng/mL的患者中,TR-SB和TP-TB2种穿刺方式对PCa和CSPCa的检出率差异无统计学意义($P>0.05$)。当tPSA水平处于4~<10 ng/mL或10~<20 ng/mL,且在游离/总前列腺特异性抗原(free/total prostate specific antigen,f/tPSA)小于0.16时,TP-TB组对PCa和CSPCa的检出率高于TR-SB组($P<0.05$),tPSA水平处于10~<20 ng/mL时,TP-TB组对CSPCa的检出率高于TR-SB组($P<0.05$)。TR-SB组和TP-TB组在并发症总发生率上无差异($P>0.05$),TR-SB组术后出现发热、感染的风险高于TP-TB组($P<0.05$)。**结论:**TP-TB在tPSA 4~<10 ng/mL、10~<20 ng/mL,且f/tPSA<0.16时具有更高的PCa检出率。当tPSA 10~<20 ng/mL,尤其同时f/tPSA<0.16时,TP-TB对高侵袭度的CSPCa有更高的检出率,且术后感染的风险更低,可作为一种高效且更安全的穿刺方法应用于临床。

【关键词】前列腺癌;前列腺特异性抗原;前列腺穿刺活检

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A comparison of the diagnostic value of transrectal and transperineal prostate biopsies for prostate cancer

Wang Linfeng, Luo Shengjun, Tang Wei

(Department of Urological Surgery, The First Affiliated Hospital of Chongqing Medical University)

【Abstract】Objective: To compare the difference in the detection rate of prostate cancer(PCa) between ultrasound-guided transrectal prostate systematic biopsy(TR-SB) and magnetic resonance/ultrasound-guided transperineal prostate targeted biopsy(TP-TB), and to evaluate the diagnostic value of both methods. **Methods:** A retrospective analysis was conducted on 310 patients who underwent transrectal and transperineal prostate biopsies in the First Affiliated Hospital of Chongqing Medical University from December 2020 to May 2022. The patients were divided into TR-SB group and TP-TB group based on the biopsy methods. The two biopsies were compared for the differences in the detection rates of PCa and clinically significant prostate cancer(CSPCa), as well as the incidence of complications. **Results:** There was no significant difference in the detection rates of PCa and CSPCa between the TR-SB and TP-TB groups in patients with a total prostate-specific antigen(tPSA) level of 4~50 ng/mL($P>0.05$). The detection rates of PCa and CSPCa were significantly higher in the TP-TB group than in the TR-SB group when the tPSA level was between 4~<10 ng/mL or 10~<20 ng/mL and the free/total prostate-specific antigen(f/tPSA) level was less than 0.16($P<0.05$). The detection rate of CSPCa was significantly higher in the TP-TB group than in the TR-SB group when the tPSA level was between 10~<20 ng/mL($P<0.05$). There was no significant difference in the overall incidence of complications between the two groups($P>0.05$). The risk of postoperative fever and infections was significantly higher in the TR-SB group than in the TP-TB group($P<0.05$). **Conclusion:** TS-TB has a higher detection rate for PCa and CSPCa in patients with a tPSA level of 4~<10 ng/mL or 10~<20 ng/mL and an f/tPSA level of less than 0.16. For patients with a tPSA level of 10~<20 ng/mL, especially accompanied by an f/tPSA level of less than 0.16, TP-TB has a higher detection rate for highly invasive CSPCa and has a lower risk of postoperative infections, making it an efficient and safer biopsy method in clinical practice.

作者介绍:王林峰,Email:857174540@qq.com,

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通信作者:唐伟,Email:tagwei2060@163.com。

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前列腺癌(prostate cancer, PCa)是老年男性最常见的恶性肿瘤,全美前列腺癌的发病率每年增加3%,新诊断的前列腺癌病例达288 300例^[1]。我国前列腺癌的发病率逐年上升,是我国男性泌尿生殖系统中发病率最高的肿瘤^[2]。

前列腺穿刺活检是诊断PCa的金标准,目前临幊上主要多采用超声引导下经直肠前列腺系统穿刺(transrectal prostate systematic biopsy, TR-SB)^[3],但在临幊应用中漏诊率较高。经会阴前列腺靶向穿刺(transperineal prostate targeted biopsy, TP-TB)常在多参数磁共振成像(multiparametric magnetic resonance imaging, mpMRI)和超声引导下进行,mpMRI可以在T2WI、DWI、DCE-MRI等序列提示前列腺异常区域^[3-5],再导入超声系统,为前列腺的精确穿刺提供依据。研究表明,前列腺活检的总并发症率为15.9%,其中最常见的并发症是脓毒血症、血尿和直肠出血^[6]。使用经直肠入路进行前列腺活检可能会增加并发症的风险,其中包括一些可能危及生命的情况,例如急性前列腺炎、败血症和严重的直肠出血。经会阴前列腺穿刺大大降低感染的风险,且可避开直肠动脉或痔疮丛的轨迹,从而提高前列腺活检的安全性^[7],且在总前列腺特异性抗原(total prostate specific antigen, tPSA)水平4~20 ng/mL时,靶向穿刺的前列腺癌检出率、敏感性、特异性和阳性预测值优于系统穿刺,阴性预测值相似^[8-10],也有研究显示采用系统穿刺和靶向穿刺对临床有意义的前列腺癌(clinically significant prostate cancer, CSPCa)的检出率无明显差异^[11]。鉴于前列腺穿刺方法的选择对PCa的检出和并发症的发生具有重要影响,本研究以此为切入点,比较TR-SB和TP-TB在PCa检出率、CSPCa检出率和并发症的差异。

1 资料与方法

1.1 一般资料

选取2020年12月至2022年5月于重庆医科大学附属第一医院泌尿外科行经直肠和经会阴前列腺穿刺的患者共310例,其中TR-SB组211例患者,TS-TB组99例患者。纳入标准:所有患者都按照《前列腺穿刺中国专家共识》有穿刺指征:①tPSA>10 ng/mL;②直肠指检发现前列腺可疑结节;③经直肠超声、MRI或PSMA PET/CT发现可疑病灶;④tPSA 4~10 ng/mL时,游离/总前列腺特异性抗体(free/total prostate specific antigen, f/tPSA)小于0.16,和(或)PSA密度大于0.15 ng/mL²,和或PSA每年升高速率大于0.75 μg/L;⑤其

他前列腺相关检测结果异常,如前列腺健康指数等。

排除标准:①tPSA≥50 ng/mL, tPSA<4 ng/mL;②通过穿刺病检或手术病检结果提示前列腺以外来源的转移肿瘤;③术前6个月内有内分泌治疗史;④既往有行前列腺电切术、前列腺根治术手术史。本研究已通过医院伦理委员会批准同意。

1.2 围术期治疗及手术过程

参照《中国泌尿外科和男科疾病诊断治疗指南》,所有前列腺穿刺活检患者术前常规预防性口服氟喹诺酮类或第一、二代头孢菌素。

TR-SB手术过程:患者取侧卧位,常规消毒、铺巾,稀碘伏灌肠消毒,肛门内注入利多卡因凝胶黏膜麻醉,在超声引导下使用穿刺活检针(嘉利VPA18/25)行经直肠前列腺12针活检穿刺。穿刺标本每条单独送病理。TP-TB手术过程:术前完成会阴区的备皮。患者取截石位,常规消毒、铺巾,会阴部皮下注射1%利多卡因局部麻醉,导入患者MRI影像数据,并对该影像进行病灶标记和穿刺设计,经直肠置入双层面超声探头,通过融合穿刺图像主机将该探头所呈现的实时超声影像和患者的MRI图像融合,显示前列腺病灶。在该融合图像引导下,采用穿刺活检针(嘉利VPA18/25)经会阴穿刺可疑病灶,之后常规在前列腺左右叶穿刺,穿刺针数12+X,X为在可疑病灶处的穿刺针数。所有穿刺过程均由同一名高年资医生完成。

术后观察患者生命体征,若无特殊异常术后第1天可办理出院,观察患者有无排尿困难、血尿、术区疼痛以及有无发热情况。对于不同程度疼痛的患者,必要时予以对症治疗;出现术后发热、全身炎症反应综合征(systemic inflammatory response syndrome, SIRS)及脓毒血症患者,常规检查中段尿培养和血培养(包括厌氧菌和需氧菌培养),给予静脉头孢菌素类或喹诺酮类抗感染药物,如果感染仍不能控制或者根据药物敏感试验结果调整抗菌药物,必要时抗菌药物升到更高级别,患者住院直至体温恢复正常后3 d可出院;尿潴留给予保留导尿;血尿和(或)血便给予止血、抗感染等对症处理。

1.3 统计学处理

采用SPSS 26.0统计软件进行数据分析处理,计数资料以百分比表示,采用Shapiro-Wilk检验各值是否呈正态分布,符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,不符合正态分布的计量资料以 $M_d(P_{25}, P_{75})$ 表示。计数资料的组间比较行卡方检验或Fisher确切概率检验;计量资料的组间比较,行t检验、非参数秩和U检验。检验水准 $\alpha=0.05$ 。

2 结 果

2.1 一般资料比较

根据排除标准,最终纳入232例患者,其中TR-SB组145例,TP-RB组87例。TR-SB组和TP-TB组在年龄、tPSA、f/tPSA上差异无统计学意义($P>0.05$),见表1。

表 1 2 组患者的一般资料 [$M_d(P_{25}, P_{75})$]

组别	年龄/岁	tPSA/(ng·mL ⁻¹)	f/tPSA
TR-TB组	68(74,62)	11.93(5.88,18.10)	0.15(0.11,0.19)
TP-TB组	70(60,80)	10.93(5.82,15.73)	0.12(0.07,0.17)
Z值	-1.172	-0.396	-0.603
P值	0.241	0.692	0.546

2.2 2 组穿刺后结果的比较

本研究将 Gleason 评分≥7 分定义为 CSPCa^[12], 同时根据 Gleason 评分结果进行国际前列腺癌分级系统分类(international society of urological pathology, ISUP)。TR-SB 和 TP-TB 2 种穿刺对 PCa 检出率、CSPCa 检出率、术后住院时间、穿刺针数的差异无统计学意义($P>0.05$), 见表 2。

表 2 2 种穿刺结果的比较 [$n, \%; M_d(P_{25}, P_{75})$]

项目	TR-SB组	TP-TB组	χ^2 值/Z值	P值
PCa检出率	41(28.3)	31(35.6)	1.375	0.241
CSPCa检出率	28(19.3)	21(24.1)	0.761	0.383
术后住院时间/d	1(1,1)	1(1,1)	-1.377	0.169
穿刺针数/针	12(11,13)	11(10,13)	-0.320	0.749

2.3 tPSA 分层下对 PCa 和 CSPCa 的检出率结果

进一步根据 tPSA 和 f/tPSA 分层, TR-SB 组和 TP-TB 组

的穿刺结果见表 3。在对 PCa 的检出率中, 仅将 tPSA 分层为 4~10 ng/mL 和 10~20 ng/mL 时, 2 组的差异无统计学意义($P>0.05$)。若同时考虑 f/tPSA 比值时, 则当同时满足 f/tPSA<0.16 时, TP-TB 组比 TR-SB 组对 PCa 的检出率更高, 差异有统计学意义($P<0.05$)。

在对 CSPCa 的检出率中, tPSA 在 4~10 ng/mL 时, 无论是否考虑 f/tPSA, 2 组检出率差异均无统计学意义($P>0.05$)。tPSA 在 10~20 ng/mL 时, TP-TB 组比 TR-SB 组对 CSPCa 的检出率更高, 且同时满足 f/tPSA<0.16 时, TP-TB 组仍然具有更高的 CSPCa 检出率, 差异有统计学意义($P<0.05$), 但 tPSA 10~20 ng/mL, 且 f/tPSA>0.16 时, 2 组 CSPCa 检出率差异无统计学意义($P>0.05$)。见表 3。

2.4 穿刺后并发症

2 组穿刺后并发症发生率的差异无统计学意义, 见表 4。因部分患者出现复合症状, 故以出现频次的形式呈现。TR-SB 组术后各并发症出现频次如下: 血尿 6 例, 需要药物治疗的疼痛 7 例, 发热、感染 16 例(尿脓毒血症 1 例), 其他尿路症状 4 例(尿潴留 1 例, 尿路刺激征 2 例, 漏尿 1 例)。TP-TB 组术后各并发症出现频次如下: 血尿 3 例, 需要药物治疗的疼痛 6 例, 发热、感染 2 例, 其他尿路症状 2 例(漏尿 2 例)。2 组在血尿、术后疼痛、其他尿路症状发生率的差异无统计学意义($P>0.05$)。TR-SB 组术后发热、感染的发生率较 TP-TB 组高, 差异有统计学意义($P<0.05$)。

表 3 各组 PCa、CSPCa 检出率比较 ($n, \%$)

项目	TR-SB组	TP-TB组	χ^2 值	P值
PCa检出率				
tPSA 4~<10 ng/mL(n=100)	9(14.5)	10(26.3)	2.131	0.144
f/tPSA<0.16	5(16.1)	9(40.9)	4.065	0.044
f/tPSA≥0.16	4(12.9)	1(6.3)	0.041	0.840
tPSA 10~<20 ng/mL(n=86)	12(14.8)	14(37.8)	1.781	0.182
f/tPSA<0.16	7(23.3)	12(50.0)	4.158	0.041
f/tPSA≥0.16	5(26.3)	2(15.4)	0.090	0.765
CSPCa检出率				
tPSA 4~<10 ng/mL(n=100)	4(6.5)	4(10.5)	0.122	0.727
f/tPSA<0.16	3(9.7)	4(18.2)	0.239	0.625
f/tPSA≥0.16	1(3.2)	0(0.0)	-	1.000 ^a
tPSA 10~<20 ng/mL(n=86)	7(14.3)	12(32.4)	4.033	0.045
f/tPSA<0.16	3(10.0)	11(45.8)	8.915	0.003
f/tPSA≥0.16	4(21.1)	1(7.7)	0.277	0.598

注:a,Fisher 确切概率法

表 4 2 组在穿刺后并发症发生率的比较 ($n, \%$)

组别	穿刺并发症	血尿	疼痛	发热、感染	尿路症状
TR-SB组	24(16.6)	6(4.1)	7(4.8)	16(11)	4(2.8)
TP-TB组	12(13.8)	3(3.4)	6(6.9)	2(2.3)	2(2.3)
χ^2 值	2.163	0.000	0.136	5.798	0.000
P值	0.141	1.000	0.712	0.016	1.000

3 讨 论

前列腺穿刺可对样本进行分级,以此确诊侵袭性更高的CSPCa,早期诊断对预防CSPCa患者的疾病进展有重要作用^[13]。系统穿刺可获取全面的活检样本,同时操作简单、成本低廉,是前列腺穿刺的经典术式^[14]。TP-TB通过结合MRI成像实现对肿瘤灶的进一步精准定位,提升约30%~50%的PCa检出率^[15~16]。经会阴途径具有较低并发症发生率,可以弥补经直肠途径对前列腺腹侧、尖部病灶的穿刺盲区^[17~18]。研究发现经会阴途径更适合结合MRI融合穿刺,从而提升PCa的检出率^[6,11,17,19]。

PSA是PCa的常规筛选手段^[20],在tPSA值的灰区(4~10 ng/mL)中,常规方法难以进行准确的PCa诊断。本研究结果中,在tPSA 4~10 ng/mL时,TR-SB和TP-TB的穿刺率较低,分别为14.5%和26.3%。f/tPSA是指游离前列腺特异性抗原(free prostate specific antigen,fPSA)与总前列腺特异性抗原(total prostate specific antigen,tPSA)的比值,前列腺癌患者的f/tPSA往往降低^[21]。根据我国目前推荐的tPSA临界值,本研究对tPSA的分层研究,发现当tPSA 4~10 ng/mL且f/tPSA<0.16时,TP-TB的PCa检出率高于TR-SB。根据既往文献的归纳^[9~10,18],本研究继续提升所纳入的tPSA值至20 ng/mL,发现当tPSA 10~20 ng/mL时,TP-TB对CSPCa的检出率高于TR-SB,当tPSA 10~20 ng/mL且f/tPSA<0.16时,TP-TB对PCa和CSPCa的检出率均高于TR-SB。Ilic D等^[22]提出PSA检测可以降低PCa患者约30%的病死率,但会导致42%过度诊断和29%过度治疗,因此建议将f/tPSA纳入分析以避免检测导致的过度诊疗^[23~24]。Mitchell IDC等^[21]发现通过f/tPSA比值可以提升25%~48%的PCa检出率,同时降低约10%的假阳性率。这些研究说明当f/tPSA降低时,即使tPSA值升高不明显,患者仍然面临危险度更高的PCa发生率。本研究结果说明当tPSA 4~20 ng/mL且f/tPSA<0.16时,TP-TB比TR-SB对PCa、CSPCa的检出率更高,弥补了TR-SB对处于该tPSA分层患者的漏诊,尤其是可以早期发现潜在的CSPCa。有学者认为tPSA水平和PCa病灶大小有一定程度正相关性^[25],tPSA灰区TP-TB阳性率更高,可能和MRI图像对前列腺内微小异常病灶的暴露有关^[16~17,19,26~27]。在tPSA 4~50 ng/mL时,TP-TB和TR-SB的PCa和

CSPCa检出率无明显差异,这可能是因为tPSA水平和病灶大小正相关^[25],且PCa的多灶性是常见的^[28],系统穿刺对病灶的覆盖率更高,从而使得两种穿刺方式对PCa的检出率无明显差异。

TP-TB组的穿刺后并发症总体发生率与TR-SB无明显差异。对并发症进行分类后,本研究发现TR-SB组发生术后发热、感染的风险明显高于TP-TB组。穿刺的物理损伤打破了前列腺的天然屏障,导致细菌在前列腺组织内扩散^[6]。研究表明,经直肠路径更容易出现感染、直肠损伤,并且穿刺过程直肠肌肉紧张也可能导致尿失禁等。而经会阴路径更容易刺激体表疼痛感受器和损伤尿道,导致疼痛和尿道狭窄等并发症^[14,17,19]。即使预防性口服抗生素并完善术前灌肠,直肠仍是一个相对富含细菌的环境,故细菌术中移植的问题难以规避。TR-SB组患者多出现复合并发症,并且有1例存在严重的感染性休克,4例出现下尿路症状的患者中存在1例尿潴留,这或许提示TR-SB组可能会导致更严重的并发症。

本研究的局限性在于它是一项回顾性研究,受限于研究队列的病例数量,后续研究有待完善和提高。

综上,TP-TB在tPSA 4~<10 ng/mL、10~<20 ng/mL,且f/tPSA<0.16时具有更高的PCa检出率。当tPSA 10~<20 ng/mL,尤其同时f/tPSA<0.16时,TP-TB对高侵袭度的CSPCa有更高的检出率,而且TP-TB术后感染的风险更低,可作为一种高效且更安全的穿刺方法应用于临床。

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