

良性前列腺增生的超微创术式研究进展

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摘 要

良性前列腺增生是我国中老年男性群体中高发的泌尿系统疾病, 以排尿功能障碍为核心临床表现。该疾病的发病率呈明显年龄相关性递增趋势, 并且近些年发现其发病年龄逐渐年轻化。想要快速缓解症状应首选外科治疗。前列腺增生外科治疗方案很多, 目前外科治疗的金标准为经尿道前列腺电切术, 该术式虽能有效缓解排尿困难等下尿路症状, 但其临床应用中仍伴随多种不可忽视的并发症包括术中出血较多、电切综合征、尿道狭窄、勃起功能障碍等, 这些问题严重影响了患者术后的就医满意度和生活质量。随着医疗技术的不断发展和以患者为中心的外科治疗理念指导下, 前列腺增生的超微创术式逐渐受到重视。本文就前列腺增生的超微创术式研究进展进行综述。

关键词

前列腺增生, 超微创术式

Research Progress of Ultra-Minimally Invasive Surgery for Benign Prostatic Hyperplasia

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Abstract

Benign prostatic hyperplasia (BPH) is a highly prevalent urinary system disease among middle-aged and elderly men in China, with urination dysfunction as the core clinical manifestation. The

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incidence of this disease shows a significant age-related increasing trend, and in recent years, it has been found that the age of onset is gradually getting younger. To relieve symptoms quickly, surgical treatment should be the first choice. There are many surgical treatment options for benign prostatic hyperplasia. Currently, the gold standard for surgical treatment is transurethral resection of the prostate (TURP). Although this surgical method can effectively relieve lower urinary tract symptoms such as difficulty in urination, it still accompanies many complications that cannot be ignored in clinical application, including excessive intraoperative bleeding, transurethral resection syndrome, urethral stricture, erectile dysfunction, etc. These problems have seriously affected patients' satisfaction with medical treatment and quality of life after surgery. With the continuous development of medical technology and under the guidance of the patient-centered surgical treatment concept, the ultra-minimally invasive surgical methods for benign prostatic hyperplasia have gradually received attention. This article reviews the research progress of ultra-minimally invasive surgical methods for benign prostatic hyperplasia.

Keywords

Benign Prostatic Hyperplasia, Ultra-Minimally Invasive Surgical Methods

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1. 引言

良性前列腺增生(Benign prostatic hyperplasia, BPH)表现为功能性的排尿异常改变, 主要机制为前列腺腺体增生引起膀胱出口梗阻, 导致后尿道延长、受压变形、狭窄和尿道阻力增加, 致使膀胱功能受损[1] [2], 从而引起下尿路症状(包括尿频、尿急、夜尿增多, 同时伴有进行性排尿困难, 进一步可出现反复尿潴留、感染、肾功能损害等情况)和生活质量下降[3] [4]。目前 BPH 的临床治疗主要包括药物治疗和手术治疗, 对于早中期下尿路症状不严重的 BPH 患者而言, 首选药物治疗[5]。其可以部分减轻或控制尿频尿急等刺激性症状, 但对于部分口服药物治疗效果较差者、拒绝接受药物治疗、中至重度下尿路症状并已明显影响生活质量的 BPH 患者而言, 常需要外科手术干预以缓解症状[6] [7]。目前 BPH 患者逐渐年轻化, 对手术微创、安全有效、术后控尿和性功能保留等需求越来越关注。近年来, 超微创术式逐渐成为 BPH 治疗的新兴技术, 并逐步成为重要治疗选择。超微创术式是指通过最小创伤、最小切除、最小损伤等方式, 达到治疗目的的微创技术。最常见类型包括前列腺尿道悬吊术、前列腺动脉栓塞术、经尿道针消融术、经尿道微波治疗热蒸汽消融术、Aquablation 等术式; 未来进展包括临时植入式镍钛装置、Optilume 等术式。这些术式具备安全有效、手术时间短、恢复快、并发症少, 缩短住院时间, 保留性功能等特点[8] [9]。本文拟对这些超微创术式进行综述, 通过现有文献总结每种超微创术式的优点及不足, 实现 BPH 的个体化治疗, 避免“一刀切”, 为临床医师决策提供理论依据。

2. 前列腺尿道悬吊术

前列腺尿道悬吊术(Prostatic urethral lift, PUL)是一种非消融技术, 在局部或全身麻醉下进行, 通过在膀胱镜引导下放置小型永久性金属植入物, 通过一次性特殊装置机械压缩两个前列腺侧叶, 从而扩大尿道腔并消除阻塞。植入物由三部分组成: 包膜片、尿道端片和缝线, 包膜片固定于前列腺包膜外; 尿道端片固定于前列腺段尿道内; 缝合线使用可调节的聚酯单丝制作[10]-[12]。Das 等[13]系统分析了 PUL 和经尿道前列腺电切术(Transurethral resection of prostate, TURP)的临床疗效及安全性差异, 结果显示 PUL、

TURP 在术后国际前列腺症状评分(International prostate symptom score, IPSS)、生活质量(Quality of life scale, QoL)、最大尿流率(Maximum flow rate, Qmax)上有明显改善, 但 TURP 在客观症状及功能改善方面更优。但在术后恢复时间、住院时间、保留性功能等方面 PUL 更具有优势。Userovici 等[14]对 40 例行 PUL 的患者进行了平均时间长达 32 个月的随访, 在 PUL 干预 3 个月后, 患者的 IPSS、QoL 显著改善, 且国际勃起功能指数(International index of erectile function-5, IIEF-5)与术前无明显差异。随着时间的推移, 泌尿功能评分的改善是稳定的, 勃起和射精功能评分也随着时间的推移保持稳定, 并且其中只有 2 名患者因尿潴留需要行导尿之外, 其余没有报道任何 Clavien-Dindo 评分 > 2 的并发症。但在对 40 例患者的随访中, 14 例患者需要额外手术治疗前列腺增生症, 总体再入院率高。Shah 等[15]比较了接受 PUL 时前列腺体积 < 80 g 和 > 80 g 的患者, 他们发现较大组需要更多植入物, 但疗效和再入院率方面无明显差异, 尽管样本量较小。PUL 适用于前列腺体积 < 70 ml, 且中叶不明显增生患者。禁忌症包括前列腺癌、中叶增生、尿道狭窄的患者。PUL 通常耐受程度高, 术后并发症轻微, 最常见的并发症包括排尿困难(9%)、盆腔疼痛(6%)、尿尿(4%)和急迫性尿失禁(3%), 且大多在手术后四周内缓解[16]。PUL 术式的操作相对较为简单, 但仍然需要一定的技术积累。对于初学者, 掌握金属植入物的精确放置是关键, 通常认为, 完成 20~30 例手术后, 学习曲线将趋于平稳。PUL 可作为日间手术进行, 通常在局部麻醉下进行, 因此总体医疗成本较低。PUL 为希望维持性功能并快速改善症状的 BPH 患者提供了安全有效的治疗方案[17]。

3. 前列腺动脉栓塞术

前列腺动脉栓塞术(Prostate artery embolization, PAE)是一项由介入放射科医师主导实施的微创治疗技术, 手术在局部麻醉下完成。首先经股动脉或桡动脉建立穿刺通路, 随后借助数字减影血管造影技术精准定位并明确前列腺的供血动脉分布, 最后将带有特殊药物的微导管沿通路送至目标血管, 对前列腺的主要供血动脉进行栓塞处理, 通过阻断血供诱导前列腺组织发生缺血性坏死及体积萎缩, 从而达到治疗目的[18]-[20]。Pisco 等[21]在对药物治疗无效的男性患者进行 PAE 与假手术比较的随机对照试验中发现, 与假手术组相比, PAE 组在术后 6 月、12 月的 IPSS 和 QoL 显著改善。Zumstein 等[22]和 Huang 等[23]对 PAE 和 TURP 进行 meta 分析发现, PAE 在 IPSS 评分、Qmax、前列腺体积和 PVR 方面显著改善, 但改善程度不如 TURP 明显, 但是 IIEF-5 在 PAE 后表现更好, 且不良事件显著降低。Knight 等[24]和 Abt 等[25]对 PAE 和 TURP 研究发现, PAE 在术中出血量少、术后恢复时间短、术后并发症发生率低等方面均有优势。Veyg 等[26]比较了 PAE 在 24 个月随访时前列腺体积为 > 80 g 与 < 80 g 的患者临床结果, 以确定 PV 是否预测 PAE 的疗效或持久性, 结果表示 PAE 对 BPH 患者既安全又持久, 并且在广泛的基线 PV 范围内都能有效。由于不同患者的前列腺动脉、侧支循环在数量上差异显著, 位置也各有不同, 且与前列腺动脉相连的腹腔血管布局复杂, 不仅对术者的技术和经验提出了较高要求, 也会在不同程度上影响患者的术后效果[27]。所以禁忌症包括血管解剖结果不良、碘造影剂过敏、严重凝血功能障碍、肾功能不全患者。由于 PAE 治疗在局麻下进行, 因此总体医疗成本相对于 TURP 而言较低。目前 PAE 的短期随访良好, 但缺乏长期研究数据, 需要大量病例和更长随访时间的研究来验证其疗效性及安全性[23]。

4. 经尿道微波治疗

经尿道微波治疗(transurethral microwave thermotherapy, TUMT)是一种门诊接受局部麻醉的微创治疗, 通过将治疗导管(导管由弯曲的尖端、温度传感器和微波单元组成。远端端口内设有膀胱气球, 便于尿液引流和冷却)插入尿道后, 通过无菌水回流和经腹或经直肠超声确认, 并对膀胱气球进行充气。利用微波诱导热量消融前列腺组织[28]-[30]。Ziętek 等[31]回顾性分析对比发现 TUMT 相较于药物治疗而言 IPSS 及 IIEF-5 均较药物治疗组有显著改善, 且 TUMT 组 24% 的患者报告勃起功能明显改善, 在验证 TUMT

的有效性的同时突出其有对性功能改善的特点, 但该研究随访时间较短。Franco 等[32]对 TUMT 与 TURP 进行比较发现, 经尿道微波热疗法在短期随访中可能对尿路症状几乎没有变化, 但对长期效果尚不确定, 且副作用的发生率明显低于 TURP。

5. 经尿道针消融术

经尿道针消融术(transurethral needle ablation, TUNA)是一种局麻下的经尿道微创技术, 其是利用低强度射频能量, 在保护尿道及邻近结构的同时, 对多增生前列腺组织进行消融坏死。尽管 TURP 仍是治疗 BPH 的金标准, 但门诊式 TUNA 因其微创性和避免全身麻醉而成为一个有吸引力的替代方案[33]。Law 等[33]收集了 121 位 BPH 患者接受 TUNA 术后一年随访数据。结果提示 TUNA 术后 IPSS、QOL、Qmax 均较术前显著改善, 仅 2 例需要再次住院治疗。Hill 等[34]对 TUNA 和 TURP 进行了长达 5 年的随访研究, 研究证实 TUNA 具有良好的安全性, 其副作用发生率低于 TURP。

6. 热蒸汽消融术

热蒸汽消融术(Water vapor thermaltherapy, WVTT)术式的开展主要基于 Rezūm 热蒸汽消融系统, 简称为 Rezūm 消融术。WVTT 于 2015 年在美国和欧洲首次被引入 BPH 的临床治疗中, 用于治疗 BPH 引起的下尿路症状。其原理是通过射频能量将液态水转化为高温热蒸汽(103℃), 精准注入前列腺组织并通过组织间隙对流扩散, 利用高温蒸汽将前列腺组织加热至约 70℃迅速杀死前列腺增生组织, 使其逐步自然萎缩并被人体自然吸收, 从而达到治疗效果。该系统应用波士顿科学公司 Rezūm 器械(Rezūm 主机(含电源开关、盐水滚轮泵、无菌水注射器支架、一次性使用前列腺热蒸汽治疗器械端口)、一次性使用前列腺热蒸汽治疗器械(灰色出针键、蓝色热蒸汽激发键、收针键、盐水冲洗键)、无菌水注射器、无菌水注射器插针接口、射频电缆、无菌水管线、排液管线、盐水冲洗管线)、30°膀胱镜、膀胱镜监视器、生理盐水等[35]-[37]。为了评估 WVTT 的疗效, McVary 等[38]对 181 名进行了 WVTT 的 BPH 患者进行了半年的随访, 结果显示 WVTT 具有令人满意的短期效果、缩短的手术时间, 并且在 IPSS、QoL、Qmax 方面有显著改善, 且不会影响性功能。对于治疗大体积 BPH 患者的研究, Bole 等[39]比较了平均前列腺尺寸为 119 cm³ 与平均尺寸为 49 cm³ 的患者使用 WVTT, 得出的结论是, 前列腺体积为 >80 cm³ 的受试者的临床症状有客观的改善, 与腺体小于 80 cm³ 的患者相当。热蒸汽消融术的不良事件发生率, 最常见报道症状是排尿困难和血尿, 但均可在术后 3 个月内缓解[40]。作为引进国内的较新技术, 目前国内对于前列腺消融术的研究还处于早期阶段, 相对应的其临床应用较少, 需要更多的长期随访中验证其疗效及安全性。TUNT、TUNA、WVTT 均是前列腺消融术, 通过能力导致前列腺消融坏死, 优点包括长期有效, 对性功能影响小及门诊化; 缺点包括缺少前列腺癌诊断能力, 符合适应证患者少。与 TURP 相比, 其可在门诊下进行, 无需麻醉, 避免了麻醉并发症的出现, 也减少了费用的消耗。手术的学习曲线较短, 操作简单, 不需要高度专业的技能, 术者完成 10~15 例手术后通常能够熟练操作。

7. Aquablation 治疗

Aquablation 水刀疗法是利用 AquaBeam 机器人系统, 在实时超声引导下应用高速水射流技术精准定位并消融前列腺组织。该技术最早由 Farber 等人于 2015 年首次使用 AquaBeam 系统进行描述。AquaBeam 水化系统包含三个主要组成部分: 配套规划单元; 机器人 24-Fr 手持装置; 还有一台控制台。该手术可在全身麻醉或脊柱麻醉下进行, 治疗过程中可对机器进行控制并且看到前列腺切除全过程[41]-[43]。Gilling 等[44]对 Aquablation 和 TURP 两组进行比较研究发现, 两者在 6 个月时 IPSS 均显著改善, 且 Aquablation 和 TURP 的手术时间相似(33 分钟对 36 分钟), 但水化切除时间显著较低(4 分钟对 27 分钟)。除此之外,

Aquablation 的射精功能障碍率较低(10%对 36%)。Gilling 等[45]研究发现 Aquablation 与 TURP 治疗 BPH 具有相似的疗效, 该研究随访时间长达三年, IPSS 平均改善分别为 14.4 分和 13.9 分, Qmax 分别提升了 11.6 mL/s 和 8.2 mL/s, 且所有患者无需再次进行手术治疗。Zorn 等[46]研究了 101 位接受 Aquablation 治疗的大体积前列腺(80~150 ml)患者, 随访 3 年期间, IPSS、Qmax、QoL、PVR 均显著改善, 验证了 Aquablation 是大体积前列腺患者有效且持久的治疗方案。Aquablation 主要的缺点是术后出血控制相对不足, 因为 Aquablation 不具备 TURP 或各种激光的凝血特性。Aquablation 需在全麻下进行, 因此针对无法承受全身麻醉的患者而言无法进行手术, 除此之外还包括前列腺癌或尿道狭窄患者。Aquablation 的学习曲线较平缓, 但需要熟悉机器人操作和超声引导技术, 建议术者至少完成 20 例手术后可达到较高的操作水平。Aquablation 的设备和技术支持较为昂贵, 缺少大样本量对照试验等限制了机器人辅助技术的普及, 其临床疗效和安全性仍然需要大规模对照研究进行验证。

8. 临时植入式镍钛装置

临时植入式镍钛装置(Temporary implantable nitinol devices, Tind)于 2015 年首次推出, 并于 2020 年获得 FDA 批准, 是一种微创治疗 BPH 的选择[47]。Tind 分为第一代和第二代, 由于第二代临时植入式镍钛设备(iTind)目前是市场上唯一的产品, 所以这里着重介绍 iTind [48]。iTind 是一种可折叠的镍钛装置, 由三根交织的金属丝臂组成(分别位于 12 点、5 点和 7 点钟方向), 通过膀胱镜插入。该装置可持续施加压力, 导致黏膜缺血和坏死, 形成 12 点、5 点和 7 点钟方向的前列腺切口, 引起前列腺尿道和膀胱颈的重塑, 放置 5 到 7 天后再通过膀胱镜手术取出[48] [49]。Chughtai 等[50]对 iTind 与假手术进行了比较, 在 12 个月时 iTind 组 IPSS 降低了 9.25 分, Qmax 值增加了 3.52 mL/s, QoL 提升 1.9 分, 且未报道新发性射精或勃起功能障碍。Amparore 等[51]对 81 例行 iTind 的患者(前列腺体积小于 75 ml 的男性)进行了长达 3 年的随访, 结果显示 iTind 治疗 BPH 的临床疗效在 3 年随访期内保持稳定, 患者的 IPSS、Qmax、PVR 等核心疗效指标均呈现持续改善趋势。安全性方面, 术后 12~36 个月的随访期间未观察到晚期并发症的发生; 性功能相关指标在 3 年随访期内维持稳定, 且无勃起功能障碍、射精功能障碍等相关不良事件的报道。所有患者在 24~36 个月期间均未接受替代治疗。iTind 目前适用于前列腺体积 < 60 ml、侧叶增生明显的患者。目前尚未在既往前列腺癌患者、突出正中叶、尿道狭窄、同时患有膀胱结石或既往前列腺手术的患者中进行此手术。虽然尚未正式评估, 但根据既往研究医生的观察和经验表明, 该手术的学习曲线较短。患者可当天出院, 只需简单止痛治疗, 5 至 7 天后, 患者回来取出装置, 可明显减少医疗成本。iTind 常见的自限性并发症包括轻度尿痛、短暂性血尿、排尿困难和急迫感。iTind 目前仅有短期和中期随访数据, 仍需进一步研究以评估 iTind 结局在长期随访中的持久性。

9. Optilume

Optilume BPH 导管系统是一种创新的、获得 FDA 批准的新型微创治疗方法, 由两根扩张球囊导管组成: 一根为无涂层的扩张前导管, 另一根为药物涂层球囊导管(所用药物称为紫杉醇, 这是一种抗增殖剂, 用于维持前列腺尿道扩张后尿道的腔通畅度)。通过球囊扩张以打开尿道腔, 随后输送紫杉醇以维持尿道通畅[52]-[54]。Kaplan 等[55]比较 Optilume BPH 系统与假手术研究发现, 在 12 个月时, Optilume BPH 系统的 IPSS、QoL 和 Qmax 较基线明显改善, 同时对性功能影响不大, 甚至有轻微提升。Kaplan 等[50]还为评估 Optilume 的疗效和安全性, 对 80 名纳入的患者进行了一年的术后随访, 结果报道 3 个月时, IPSS 较基线改善≥40%的受试者在 3 个月和 1 年时为 81%。IPSS 从基线的 22.3 提升到 1 年后的 7.9, Qmax 从 10.9 mL/s 提升到 18.4 mL/s, IPSS 生活质量从 4.6 提升到 1.3, 所以指标均有持久改善, 术后未报告新发射精或勃起功能障碍。患者选择方面应排除既往微创或手术性前列腺干预、膀胱内前列腺突出>1

cm、神经源性膀胱、尿道狭窄等。Optilume BPH 系统最常见的不良反应为血尿、尿路感染、排尿困难和急迫性/混合性尿失禁,一般在4周内缓解。尽管Optilume目前尚未被纳入指南,但现有的疗效数据显示其效果持久且安全性可接受,且其无需全身麻醉,可通过在门诊进行,降低了患者的医疗成本。持续和未来的研究将进一步完善其长期安全性和有效性。

10. 总结

随着医疗技术的持续革新和微创理念的不断发展,以超微创治疗为代表的新型术式不断涌现,如PUL、PAE、TUNA、TUMT、WVTT、Aquablation、iTind、Optilume等术式。现有研究显示,这些技术均能不同程度改善IPSS、QoL及Qmax,并在减少术中出血、降低并发症、缩短恢复时间和保留性功能等方面更具有优势,已成为特定人群的重要治疗选项。PUL适用于前列腺体积<70 ml,且中叶不明显增生患者;PAE适用于那些因前列腺体积过大或高危高龄的患者;TUNA适用于前列腺体积<50 ml患者;TUMT适用于前列腺体积<100 ml患者;WVTT建议前列腺体积<80 ml但针对大前列腺体积患者仍然有效;Aquablation在大体积前列腺患者中表现突出;iTind适用于侧叶增生明显患者;Optilume适用于前列腺体积<80 ml患者。然而,当前各超微创术式的长期疗效证据仍较为有限,不同技术之间缺乏直接对比研究,且对于大体积前列腺及复杂解剖患者的最佳治疗策略尚存争议。未来的研究应聚焦于开展多中心随机对照试验,延长随访周期,提升真实世界研究数据,并进行成本效益分析,以进一步明确各技术的优势、局限性及适应症,推动BPH治疗的规范化与个体化发展。

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