

·指南解读·

《加拿大泌尿外科学会男性下尿路症状/ 良性前列腺增生指南更新》解读

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摘要: 良性前列腺增生 (benign prostatic hyperplasia, BPH) 是中老年男性常见的排尿障碍性疾病,也是泌尿外科临床诊疗中最为常见的疾病之一。下尿路症状 (lower urinary tract symptoms, LUTS) 主要包括储尿期症状 (尿频、尿急、尿失禁及夜尿增多等)、排尿期症状 (排尿等待、排尿困难及排尿间断等) 以及排尿后症状 (尿不尽感、尿后滴沥等)。导致LUTS的原因除了BPH以外,还包括膀胱功能障碍、尿道及周围组织异常等。随着对BPH及LUTS的深入研究,以及循证医学的发展,各国泌尿外科学会BPH诊治指南的重心,从过去以BPH产生梗阻的解剖结构及病理诊治为主,转向了以LUTS症状学诊治为主。2022年4月由ELTERMAN等发表在*Canadian Urological Association Journal*上的“加拿大泌尿外科学会男性下尿路症状/良性前列腺增生指南更新”一文,通过对2018版加拿大泌尿外科学会BPH诊治指南的更新,总结了继发于BPH的男性LUTS的最新诊治策略。本文对该指南更新内容进行介绍及解读。

关键词: 良性前列腺增生; 下尿路症状; 坦索罗辛; 非那雄胺; 经尿道前列腺电切术

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Interpretation of UPDATE-Canadian Urological Association guideline: male lower urinary tract symptoms/benign prostatic hyperplasia

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Abstract: Benign prostatic hyperplasia (BPH) is a common urination disorder in middle-aged and elderly males, which is one of the most common diseases in urological clinical diagnosis and treatment in the world. Lower urinary tract symptoms (LUTS) mainly include storage symptoms (frequency, urgency, urinary incontinence and increased nocturnal ruination, etc.), voiding symptoms (urinary waiting, dysuria and interrupted urination, etc.) and post-voiding symptoms (urinary insufficiency, post-voiding dripping, etc.). In addition to BPH, causes of LUTS also include bladder dysfunction, urethra and surrounding tissue abnormalities. With the in-depth study of BPH or LUTS and the development of evidence-based medicine, the focus of BPH diagnosis and treatment guidelines of urological societies in various countries has shifted from the anatomical structure and pathology of obstruction caused by BPH to the symptomatological diagnosis and treatment of LUTS. UPDATE-Canadian Urological Association guideline: Male lower urinary tract symptoms/benign prostatic hyperplasia, published in the *Canadian Urological Association Journal* by Elterman et al. at April 2022, updated the 2018 edition of the Canadian Society of Urological Surgery guidelines for diagnosis and treatment of BPH, and summarized the latest diagnosis and treatment strategies for male LUTS secondary to BPH. The article introduces and interprets the updated content of the guideline.

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Keywords: Benign prostatic hyperplasia; Lower urinary tract symptoms; Tamsulosin; Finasteride; Transurethral resection of the prostate

2022年4月由ELTERMAN等^[1]发表在 *Canadian Urological Association Journal* 上的“加拿大泌尿外科学会男性下尿路症状/良性前列腺增生指南更新”一文,通过对2018版加拿大泌尿外科学会(Canadian Urological Association, CUA)良性前列腺增生(benign prostatic hyperplasia, BPH)诊治指南的更新,总结了继发于BPH的男性下尿路症状(lower urinary tract symptoms, LUTS)的最新诊治策略^[2]。文中的信息包括对2010版指南的评审,以及从更新的MEDLINE中检索英文文献进一步获得的信息,也包括对最新的美国泌尿外科学会(American Urological Association, AUA)^[3]和欧洲泌尿外科学会^[4]指南的评审。该指南是针对50岁以上出现LUTS和良性前列腺增大(benign prostatic enlargement, BPE)和/或良性前列腺梗阻(benign prostatic obstruction, BPO)的典型男性患者。与BPO以外的原因相关的男性LUTS可能需要更广泛的诊断检查和不同的治疗考虑。指南更新力求使其适用于所有正在经受LUTS或患有BPE的患者。

该指南更新同时阐述了诊断和治疗两方面的问题。诊断指南描述了以下内容:必要项目,推荐项目,可选择项目以及不推荐项目。诊断指南的推荐项目以及治疗原则基于加拿大泌尿外科医师普遍认同的临床规范和(或)专家共识而建立。诊断性建议不提供推荐等级。治疗指南使用GRADE^[5]分类法总结证据并提出治疗建议。

1 诊断指南

委员会建议对2018年CUA的BPH指南^[2]中概述的涉及诊断的因素进行轻微修订。

1.1 必要项目 必须进行评估的项目包括:病史,体格检查[含直肠指诊(digital rectal examination, DRE)],尿常规。

在对LUTS患者的初步评估中,必须进行症状严重程度和烦恼程度的评估。需要了解既往和现患的相关疾病,手术史和创伤史,目前用药情况,含非处方药和植物治疗制剂。有侧重的查体,包括DRE。尿液分析为必需项目以排除BPH以外可能导致LUTS的诊断,这些诊断通常需要另外的诊断性测试^[2-4,6-8]。

1.2 推荐项目

1.2.1 症状量表(包括烦恼程度评估) 在首次就诊中推荐使用规范的症状量表,比如国际前列腺症状评分(international prostate symptom score, IPSS),或者美国泌尿外科学会症状指数(AUA Symptom Index, AUA-SI),作为相对客观的症状评价体系,同时也用来对等待观察患者进行症状发展的随访手段,以及用作对治疗效果的评估^[9-12]。

1.2.2 前列腺特异性抗原 建议进行前列腺特异性抗原(prostate-specific antigen, PSA)检测的情况包括:预期寿命超过10年,合并前列腺癌将会改变治疗方法,PSA检测结果可能影响治疗决策。对于非前列腺癌患者,血清PSA也可作为前列腺大小的可用的替代标志,可预测BPH的进展风险^[13-14]。

1.3 可选择项目 在医生认为诊断尚不确定的情况下,可以选择进行以下项目检查:血清肌酐、尿细胞学、尿流率、残余尿量(postvoid residual, PVR)、排尿日记、50岁以上夜尿症男性进行阻塞性睡眠呼吸暂停筛查(STOP BANG 问卷调查法)、性功能问卷调查。

1.4 不推荐项目 在对BPH相关LUTS的典型患者进行常规初步评估时,不建议采用以下检查:细胞学,膀胱镜,尿动力学检查,上尿路放射学检查,前列腺超声,前列腺活检。只有在有其他适应证时,如血尿、诊断不明、DRE异常、对药物治疗效果不佳或计划手术,可能需要进行这些检查。图1总结了典型男性MLUTS/BPH患者的诊断步骤。

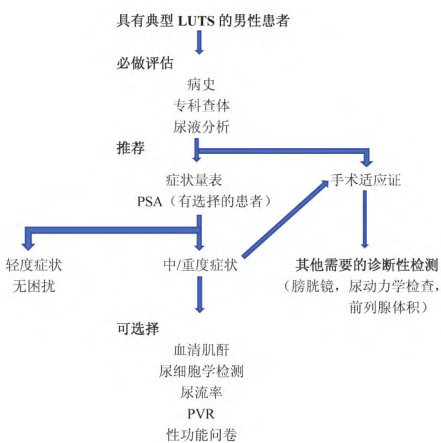


图1 典型男性下尿路症状/良性前列腺增生患者诊断的检查步骤选择

注: LUTS为下尿路症状; PSA为前列腺特异性抗原; PVR为残余尿量。

1.5 考虑手术者的进一步检查

1.5.1 手术适应证 MLUTS/BPH外科手术适应证^[2-4]包括:①反复的或难治性尿潴留;②反复性尿路感染(urinary tract infection, UTI);③膀胱结石;④反复血尿;⑤BPH继发的肾功能不全;⑥药物治疗后仍然症状恶化;⑦患者选择。膀胱憩室不能作为手术的绝对指征,但伴有复发性UTI或进行性膀胱功能障碍者可考虑。

1.5.2 术前检查 前列腺大小和中叶范围的测定与手术适应证有关(见手术治疗部分)。对于计划手术者,应进行膀胱镜检查以评估前列腺大小,以及是否存在显著的前列腺中叶增生和(或)膀胱结石。推荐超声检查用于确定前列腺的体积和中叶增生程度,以便选择合适的手术治疗方式,也可用近期的CT或磁共振成像(magnetic resonance imaging, MRI)代替。

2 治疗指南

2.1 治疗原则 治疗决策应根据症状的严重程度、困扰程度和患者的偏好来制定。向患者充分解释治疗方案的获益和风险,邀请患者尽可能多地参与共同决策,以确定最适合治疗方案。这可以通过使用CUA的BPH手术决策辅助工具来完成^[15]。轻症(IPSS <7) BPH患者,建议调整合适的生活方式并观察等待。症状轻但困扰程度严重的患者则应进一步评估。中度(IPSS 8~18)和重度(IPSS 19~35) BPH患者,治疗方案包括观察等待并调整生活方式,以及药物、微创或手术治疗。医生应根据基线年龄、LUTS严重程度和前列腺体积来告知患者症状进展的风险,如急性尿潴留(acute urinary retention, AUR)或未来需要BPH相关的手术。对于症状尚未对生活造成明显困扰的患者,建议可以通过改变不同的生活方式以减轻症状,包括:限制液体摄入量,尤其在临睡前;避免含咖啡因的饮料、酒精和辛辣食物;避免/监测某些药物(如利尿剂、血管舒张剂、抗组胺药、抗抑郁药);定时或有计划的排尿(膀胱再锻炼);避免或治疗便秘;减肥并且预防或治疗与代谢综合征相关的疾病;疑似非松弛性盆底功能障碍(可引起LUTS,盆腔和/或生殖器疼痛,肠道和性功能障碍等)或膀胱过度活动和(或)尿失禁(凯格尔运动,冲动抑制等)的盆底物理治疗。

2.2 治疗后随访

2.2.1 观察等待 处于观察等待状态的患者应定期接受医生监护,以监测任何与BPO相关的并发症。

医生应评估患者烦恼程度的进展情况,如IPSS之类的问卷式调查(主观的),或者评估排尿功能的恶化情况,如尿流率或PVR测定(客观的)。

2.2.2 药物治疗 开始接受药物治疗的患者应进行随访,以评估药物的疗效和不良反应。

2.2.3 手术治疗 接受前列腺增生手术的患者应在拔除尿管后4~6周进行复查,以评价疗效(包括症状评估,比如IPSS;有指征者进行尿流率及PVR的测定);并审查副反应和不良事件。泌尿外科医生和(或)初级保健医生将根据患者的具体情况和所采用的外科手术类型决定是否要进一步随访。

2.3 药物治疗 相较于2018版指南,专家委员会对应用 α -受体阻滞剂和/或5 α -还原酶抑制剂(5-ARIs)治疗BPH和MLUTS的管理建议进行了小的修改。因为自2018版指南发布以来,新的证据表明关于治疗MLUTS的其他药物疗法有了新的发现,即 β -3激动剂。

2.3.1 α -受体阻滞剂 阿呋唑嗪、多沙唑嗪、坦索罗辛、特拉唑嗪和塞洛多辛都可用于治疗BPH继发的LUTS^[13-24]。应用多沙唑嗪和特拉唑嗪需要剂量控制并监测血压。 α -受体阻滞剂不会改变BPH的自然进程(不能阻止前列腺体积的增长,也不降低尿潴留的风险和BPH相关手术概率)。与 α -受体阻滞剂相关的最常见不良反应是头晕(发生率2%~10%,其中特拉唑嗪和多沙唑嗪的头晕发生率最高),而坦索罗辛和塞洛多辛在射精障碍方面不良反应发生率相对较高。在使用 α -受体阻滞剂的患者中,特别是应用坦索罗辛者,有报告出现虹膜松弛综合征的不良反应;但是对于没有计划进行白内障手术的男性来说,这似乎不是一个问题,因为可以将患者正在服用这类药物及发生虹膜松弛综合征的情况告知眼科医生,并由眼科医生进行诊治^[25]。虽然这些药物的不良事件发生情况存在差异,但以上五种药物似乎具有相同的临床疗效。用药选择应取决于患者的合并症、副反应情况和耐受性。“因此,对于因前列腺增生的症状而产生生活困扰并渴望得到治疗的男性患者,推荐将 α -受体阻滞剂作为最佳的一线治疗选择(强烈推荐,证据级别A)。”

2.3.2 5 α -还原酶抑制剂 一些研究表明,应用5-ARIs治疗前列腺增生,除了能够改善症状,还能在一定程度上(25%~30%)缩小前列腺体积,并通过降低AUR发生风险和减少手术干预的需求,从而改变BPH的自然病程^[26-27]。5-ARIs主要对于前列腺体积>30 ml(和/或PSA>1.5 ng/ml)的患者有效

果。与应用5-ARIs治疗相关的不良反应主要有勃起功能障碍、性欲下降和射精障碍；另外，少数患者有男性乳腺发育和非那雄胺后综合征^[28]。“对于伴有明显前列腺增大的LUTS患者，推荐5-ARIs（度他雄胺和非那雄胺）作为可选择的有效治疗手段（强烈推荐，证据级别A）。”

2.3.3 联合治疗（ α -受体阻滞剂和5-ARIs） 提示BPH进展风险的预后因素^[29-30]包括：血清PSA>1.4 ng/ml，年龄>50岁，前列腺体积>30 ml。临床试验结果表明，与单一治疗方案相比，联合治疗显著改善症状评分并提高峰值尿流率。联合药物治疗能够降低尿潴留和（或）前列腺手术风险，但同时也因为双重治疗而增加了不良反应的发生（尤其是射精障碍）^[31-32]。“建议将 α -肾上腺素受体阻滞剂和5-ARIs联合应用，作为伴有前列腺增大（体积>30 ml）症状性LUTS患者的合适且有效的治疗策略（强烈推荐，证据级别B）。”在联合治疗6~9个月后获得成功控制的患者，可以考虑中断 α -受体阻滞剂^[33-34]。“建议联合治疗成功的患者可以选择停止使用 α -受体阻滞剂。但如果症状复发，则应该重新开始 α -受体阻滞剂的治疗（可选择推荐，证据级别B）。”

2.3.4 M受体拮抗剂和 β -3受体激动剂 储尿期症状（尿急、尿频、夜尿症）是BPH相关的男性下尿路症状中令人烦恼的部分。M受体拮抗剂（抗胆碱能药物）和 β -3激动剂已被证明能够改善男性储尿期LUTS（伴有或不伴有BPH），包括减少尿频、尿急和急迫性尿失禁的发生^[35-36]。对当代的M受体拮抗剂类药物如托特罗定和非索罗定以及 β -3激动剂米拉贝隆的研究，均显示尿潴留发生率较低，但对老年男性和伴有明显的膀胱出口梗阻（bladder outlet obstruction, BOO）的患者（PVR>250~300 ml，因为在PVR较高的男性患者中缺少安全性证据），需要慎重选用。“建议M受体拮抗剂或 β -3激动剂可用于以储尿期症状为主的BPH患者，但对于有明显的BOO和（或）PVR升高的患者应慎用（可选择推荐，证据级别C）。”

2.3.5 M受体拮抗剂或 β -3激动剂与 α -阻滞剂联合应用 混合型LUTS（既有储尿期症状也有排尿期症状），可以通过 α -受体阻滞剂与M受体拮抗剂或 β -3激动剂联合治疗，获得安全有效的治疗效果。临床试验研究了以下药物组合：坦索罗辛0.4 mg+索利那新5 mg，坦索罗辛0.4 mg+托特罗定4 mg，坦索罗辛0.4 mg+米拉贝隆50 mg^[37-42]。证据表明，联合

疗法可显著改善储尿期症状，但没有临床或统计学证据表明最大尿流率（maximum flow rate, Q_{max}）下降或尿潴留风险增加。但应除外PVR>200 ml或既往有AUR的患者。“建议对于既有排尿期症状又有储尿期症状且 α -受体阻滞剂单药治疗失败的男性LUTS/BPH患者， α -受体阻滞剂联合M受体拮抗剂或 β -3激动剂治疗，或许有效（可选择推荐，证据级别B）。”

2.3.6 磷酸二酯酶5抑制剂 磷酸二酯酶5抑制剂（phosphodiesterase type 5 inhibitors, PDE5Is）已被证实不仅能改善勃起功能，也是男性LUTS的有效治疗方法。由于具有较长的半衰期，他达拉非5 mg/d，被批准用于MLUTS。研究表明，（该药治疗）对于IPSS、储尿期和排尿期症状，以及生活质量均有改善^[43]。证据表明，PDE5Is和 α -受体阻滞剂联合治疗对于有排尿期症状合并勃起功能障碍的男性患者，疗效优于单独使用 α -受体阻滞剂^[44]。“推荐长效PDE5Is作为患有LUTS/BPH的男性患者的单药治疗方案，尤其是同时患有LUTS和勃起功能障碍的男性（强烈推荐，证据级别B）。”

2.3.7 去氨加压素 夜间多尿症（nocturnal polyuria, NP）通常与MLUTS和BPH共存，但可能对经典的BPH药物治疗无效。NP是遗尿症的主要诱发因素，国际尿失禁学会将其定义为睡眠期间的尿量异常增多。更确切地说，就是指在每日总尿量保持正常的情况下，每日排尿总量的33%发生在夜间。去氨加压素通过减少NP患者的总尿量，同时也减少了夜间排尿量，从而增加不受干扰的睡眠时间^[45]。治疗前必须检查基线血钠水平，同时应用去氨加压素注射剂或≥65岁患者口服50 μ g分散片剂的，必须在治疗开始后的4~8 d和30 d分别检查血钠。对于主要症状为夜尿症且对行为治疗措施或其他单一疗法无效的患者，应考虑应用去氨加压素。“推荐去氨加压素作为因NP导致遗尿症的LUTS/BPH患者的治疗选择（可选择性推荐，证据级别B）。”

2.3.8 植物制剂 一些患者可能会接受植物制剂治疗，常见的植物制剂包括锯叶棕（锯棕榈）、非洲刺李（非洲李子树皮）和异株荨麻（刺荨麻）。植物制剂疗法缺乏一致的配方、可预测的药代动力学和管制监督。大量研究和Cochrane荟萃分析显示，通过衡量AUA-SI、峰值尿流率、前列腺体积、残余尿量、PSA或生活质量发现，植物制剂疗法和安慰剂之间没有显著差异^[46-49]。虽然植物制剂疗法很少有副

反应,但有重要的潜在药物相互作用。“不建议将植物制剂疗法作为MLUTS/BPH的标准治疗(强烈推荐,证据级别B)。”

2.4 手术治疗

2.4.1 经尿道前列腺电切术(transurethral resection of the prostate, TURP) 单极TURP(M-TURP)仍然是前列腺体积30~80 ml并且因BPH导致中-重度LUTS患者的主要标准参考手术选择^[50]。随着时间的推移,围术期死亡率逐渐下降,目前约为0.1%,而且死亡病例的发生与前列腺体积相关(特别是>60 ml)^[51]。目前报道的并发症包括:出血(2%~9%),包膜穿孔伴明显尿外渗(2%),TUR综合征(0.8%),尿潴留(4.5%~13%),感染(3%~4%),败血症(1.5%),尿失禁(<1%),膀胱颈挛缩(3%~5%),逆行射精(65%),勃起功能障碍(6.5%),需要再次手术(2%/年)^[52-53]。“推荐M-TURP作为前列腺体积30~80 ml的中重度LUTS/BPH患者的标准一线手术治疗(强烈推荐,证据级别A)。”双极TURP(B-TURP,包括双极等离子汽化切除术)可替代M-TURP作为继发于BPH的中重度LUTS患者的手术治疗选择,与M-TURP具有相似的疗效,但围术期并发症发生率较低^[53-55]。M-TURP和B-TURP的主要区别是,B-TURP能够降低围术期出血和TUR综合征的发生风险。B-TURP的选择应基于设备可用性、外科医生经验和患者偏好。“推荐B-TURP作为前列腺体积30~80ml的中重度LUTS/BPH患者的标准一线手术治疗选择(强烈推荐,证据级别B)。”

2.4.2 开放性前列腺摘除术 开放性前列腺摘除术(open simple prostatectomy, OSP)适用于前列腺体积>80 ml且有明显症状困扰的中至重度LUTS患者^[56]。OSP的适应证还包括需同时进行其他膀胱手术,如膀胱憩室切除术或膀胱切开取石术(适用于巨大膀胱结石),以及因严重髋关节疾病而无法摆截石位的患者^[57]。OSP侵入性较强,住院周期和导尿管留置时间较长。报道估计输血率为7%~14%,并发症包括短暂性尿失禁(8%~10%)、膀胱颈挛缩和尿道狭窄(5%~6%)^[56-57]。“对于前列腺体积>80 ml的中度至重度LUTS/BPH患者,当无法进行前列腺解剖内镜下剜除术(anatomic endoscopic enucleation of the prostate, AEEP)(见下文)时,建议将OSP作为一线手术治疗选择(强烈建议,证据级别A)。”

2.4.3 微创前列腺摘除术 随着微创手术的出现,从腹腔镜开始,到机器人辅助腹腔镜,OSP也得到

了自然的发展。这些技术仍然相对较新。腹腔镜下前列腺摘除术(laparoscopic simple prostatectomy, LSP)和机器人辅助腹腔镜前列腺摘除术(robot-assisted simple prostatectomy, RASP)与OSP一样,适用于前列腺明显增大(>80~100 ml)且有严重症状困扰的LUTS患者^[58-59]。另外,也适用于伴随其他病变如膀胱巨大结石或膀胱憩室者。目前还没有随机对照试验将LSP和RASP与OSP或其他前列腺摘除术进行比较。大规模的回顾性系列研究比较了这两种手术方式,并已表明二者均安全有效^[60]。新近的一项系统综述发现,RASP与前列腺激光汽化术和切除术在IPSS、PVR、Qmax和生活质量改善方面具有相似的效果,同时在并发症发生率和估计失血量(estimated blood loss, EBL)方面也基本相同^[61]。与OSP相比,RASP的住院时间(length of stay, LOS)和EBL明显较低^[62]。但是,与激光前列腺切除术相比,RASP的导尿管留置时间和LOS更长^[61]。“推荐在有高水平机器人技术或腹腔镜手术专家的医学中心,LSP或RASP可作为前列腺体积>80 ml的中重度LUTS/BPH患者的替代手术治疗(可选择性推荐,证据级别B)。”

2.4.4 前列腺解剖内镜下剜除术 AEEP采用OSP的原理,但是需要用到不同的能源和仪器设备。可用的能源设备包括钬激光(HoLEP,含或不含摩西技术)、绿激光(GreenLEP)、单极(MonoLEP)、双极(BipoLEP)、二极管激光(Di-LEP)、钪激光(ThuLEP)和钪光纤激光(ThuF-LEP)。无论使用何种能源,AEEP的有效性和安全性已得到广泛证明^[63]。与TURP和OSP相比,AEEP在IPSS、Qmax和PVR方面有更大的改善。AEEP可以去掉更多的前列腺增生组织,同时减少出血量,缩短留置导尿管时间和住院时间^[64]。现有的证据还支持AEEP能够用于正在接受抗凝血(anticoagulant, AC)或抗血小板(antiplatelet, AP)治疗的BPH患者^[65-67]。AEEP已证明效果持久,在长达18年的长期随访中,再次手术率仅为0~3.7%(归因于前列腺腺体组织再生)^[68-72]。该手术需要术者较长的学习曲线(估计至少20~50例)^[73]。“对于任何前列腺体积>30 ml的中重度LUTS患者,如果由接受过AEEP训练的外科医生进行手术,建议可使用AEEP替代TURP或OSP。在接受AC或AP治疗的患者中,进行AEEP仍然是安全的(强烈推荐,证据级别A)。”

2.4.5 光选择性前列腺汽化术 (photoselective laser vaporization of prostate, PVP) 绿激光前列腺汽化术 (180W XPS系统和120W HPS系统) 在IPSS和Qmax的持久改善方面表现出与TURP相当的结果, 并且总体并发症发生率也相似^[74]。XPS的5年中期疗效持久性研究报告了在前列腺平均体积80 ml的患者中出现了1.1%再治疗率^[75]。在GOLIATH国际的多中心随机对照试验中, 比较了180W XPS PVP与TURP在治疗前列腺体积30~80 ml的患者的术后早期发生不良事件的情况, 尤其是出血相关的不良事件, 结果显示XPS PVP治疗组在术后前30天内不良事件的发生方面具有一定优势, 且有统计学上的显著差异^[69, 76]。与TURP相比, PVP具有更好的围术期安全性, 留置导尿管时间和住院时间均更短^[77]。多项研究表明对于伴有明显的合并症、中叶较大以及接受持续性AC/AP治疗的高龄患者, PVP治疗是安全有效的, 输血率几乎可以忽略不计^[78-82]。绿激光不仅安全性好, 在加拿大, 从经济性考虑, PVP也能成为TURP的替代^[83]。PVP不存在前列腺体积和形状的限制, 只是外科医生的专业知识和临床判断对前列腺大小的选择有一定限制。“对于中重度LUTS患者, 推荐可用PVP替代M-TURP或B-TURP (基于高质量证据的强烈推荐)。同时还建议绿激光PVP可以作为抗凝治疗或有较高的心血管风险患者的替代手术治疗方法 (可选择性推荐, 证据级别B)。”

2.4.6 经尿道前列腺切开术 (transurethral incision of the prostate, TUIP) TUIP适用于前列腺体积<30 ml且没有中叶增生的患者^[84]。与TURP相比, TUIP在症状和尿流率等排尿参数改善上具有一定优势, 而逆行射精和电切综合征的发生风险则降低 (分别为18.2%和0%); 但是, BPH相关的LUTS再手术治疗的风险显著增加, 分别为TUIP (18.4%)、TURP (7.2%)。“推荐TUIP用于治疗前列腺体积<30 ml且无中叶增生的中重度LUTS患者。患者应被告知这种治疗方式有较高的复发率并需要再手术治疗 (强烈推荐, 证据级别B)。”

2.4.7 微创技术 经尿道微波治疗 (transurethral microwave therapy, TUMT) 是有严重合并症或较高麻醉风险的老年患者的一种治疗选择, 因为该手术可以在局部麻醉下进行^[85-86]。虽然已有短期内LUTS症状改善的成功报道, 但TUMT的长期持久性效果有限, 5年累积治疗率达42%~59%^[87]。对于

中叶增生明显的患者, 不应进行TUMT。“建议将TUMT作为严格筛选且充分知情同意的患者可考虑的治疗选择 (选择性推荐, 证据级别C)。” ①前列腺支架: 对于暂时无法手术的患者, 临时性支架可以获得短期的BPO缓解^[88]。但由于LUTS加重和形成覆盖膜, 支架容易出现异位、发生移位, 并且耐受性差。考虑到这些常见的副反应, 前列腺支架在治疗中重度LUTS中的应用有限。新一代的支架目前正在测评中, 并有可能在将来为BPH/LUTS的治疗提供另一种手术选择。“建议前列腺支架仅作为膀胱逼尿肌功能正常但不适合手术治疗的患者的导尿管替代方案 (可选择性推荐, 证据级别C)。” ②前列腺悬扩术 (通过一种小型的带有永久性缝线的镍钛诺贴片植入物, 在膀胱镜引导下送入尿道前列腺部对病变的前列腺侧叶进行挤压), 简称UroLift, 与TURP相比, 虽然IPSS和Qmax的改善效果略差, 但作用充分且持久, 同时还能保留患者性功能 (12个月的观察未见逆行射精的报道)^[89]。主要的并发症包括排尿困难 (34%)、血尿 (26%)、盆腔疼痛 (19%)、急迫性尿失禁 (7%) 和尿路感染 (3%), 但这些并发症都较轻微, 并且能在4周内好转, 5年内再手术治疗的比率为13.6%^[90]。最近的一项研究 (MedLift研究) 报道了前列腺悬扩术在中叶增生患者中的应用。对于前列腺中叶增生, 突入膀胱内组织被拉入前列腺窝并固定在尿道的两侧。44名患者接受了这项技术治疗, 结果与关键的L.I.F.T.试验非常相似, 在保留射精功能的同时, IPSS降低, 生活质量提升。但需要注意的是, 这项研究的随访时间仅为12个月^[91]。“建议前列腺悬扩术 (UroLift) 可作为有意愿保留射精功能且前列腺体积<80 ml的LUTS患者的替代治疗方法。前列腺悬扩术也可用于中叶轻到中度增生并有烦恼的LUTS的患者。不论有无中叶增生, 患者均应意识到该治疗方法的5年再治疗率较高 (选择性推荐, 证据级别C)。” ③前列腺水蒸气消融术: 使用Rezum系统 (运用对流能量转移的热力学原理) 的消融治疗, 报告治疗后3个月IPSS和Qmax有显著改善, 并持续到12个月, 同时保留了勃起和射精功能^[92-93]。最新的5年研究结果证实了其持久性的疗效, 包括IPSS降低了57%, 生活质量提高了45%, Qmax提高了44%, 5年的手术再治疗率仅为4.4%^[94]。“建议Rezum系统水蒸气消融术可作为有意愿保留射精功能的前列腺体积<80 ml的LUTS患者的替代治疗方法, 包括有前列腺中叶增生的患者 (可

选择性推荐, 证据级别C。” ④前列腺高能水切割/消融术: 水消融术(利用高能水切割原理有效地切除前列腺实质组织, 同时保留血管和外科包膜等胶原结构)在前列腺体积<80 ml的患者中, 与TURP在疗效和安全性方面结果相当^[95-96]。另外的研究也证明了其在前列腺体积80~150 ml患者中的有效性和安全性。水消融术分别在近100%的患者中达到保留勃起功能目标, 约90%的患者保留了射精功能, 并且其5年再治疗率(6%)很低。“建议对有意愿保留射精功能且前列腺体积<150 ml、有或没有中叶增生的LUTS患者给予前列腺水消融术治疗(可选择性推荐, 证据级别C)。” ⑤临时性镍钛合金/支架植入术是植入一种临时的(通常5天, 之后需在局麻下取出)机械性支架状装置, 该装置通过加压使组织缺血坏死来重塑膀胱颈和前列腺部尿道达到治疗目的。3项前瞻性随机临床试验共纳入了269例进行iTind治疗的患者, 结果显示, 该治疗方法IPSS降低45%~60%, Qmax增加50%~110%, 勃起或射精功能无变化, 3年再治疗率为9%^[97-99]。远期效果的研究尚在进行中。“建议有意向保留射精功能的前列腺体积30~80 ml的LUTS患者, 可选择使用iTind。但应该让患者知晓其有较高的3年再治疗率(可选择性推荐, 证据级别C)。” ⑥前列腺动脉栓塞(prostatic artery embolization, PAE)需要由介入放射学医生在专业的介入治疗中心进行。与基线相比, PAE在12个月时IPSS、Qmax和PVR均有显著改善; 但效果

不如TURP或OSP^[100-104]。尽管PAE报道的并发症比TURP少, 但非靶向栓塞可能导致罕见的缺血性并发症, 如短暂性缺血性直肠炎、膀胱缺血、尿道和输尿管狭窄或精囊缺血^[105]。PAE用于前列腺体积>80 ml的患者疗效更佳, 可考虑作为前列腺源性肉眼血尿的治疗方法^[106-107]。在具有泌尿学和放射学合作且擅长介入治疗技术的医学中心, 对于一些经过严格筛选并且充分知情同意的患者, 如果患者愿意考虑替代治疗方案, 可以向他们提供PAE治疗。同时患者应被告知远期效果可能无法长久维持(可选择性推荐, 证据级别C)。图2和图3总结了MLUTS/BPH患者的诊治流程。

2.5 合并特殊情况的诊治

2.5.1 急性尿潴留 数据表明, AUR患者在留置尿管期间应用α-受体阻滞剂(特别是坦索罗辛、阿呋唑嗪和塞洛多辛)将增加拔除尿管后成功排尿的机会, 而加用5-ARIs可能降低未来前列腺手术的风险^[31-32, 108-110]。“建议对于因BPH导致AUR的患者, 在留置尿管期间可给予α-受体阻滞剂治疗(可选择性推荐, 证据级别B)。”

2.5.2 膀胱逼尿肌收缩力不足/下降 膀胱逼尿肌收缩力不足(detrusor underactivity, DU)被定义为膀胱逼尿肌收缩强度和(或)持续时间降低, 导致膀胱排空时间延长和(或)无法在正常时间内实现膀胱完全排空^[111]。目前还没有针对DU的有效治疗方法。原发性DU的治疗方法应是促进膀胱排空, 识

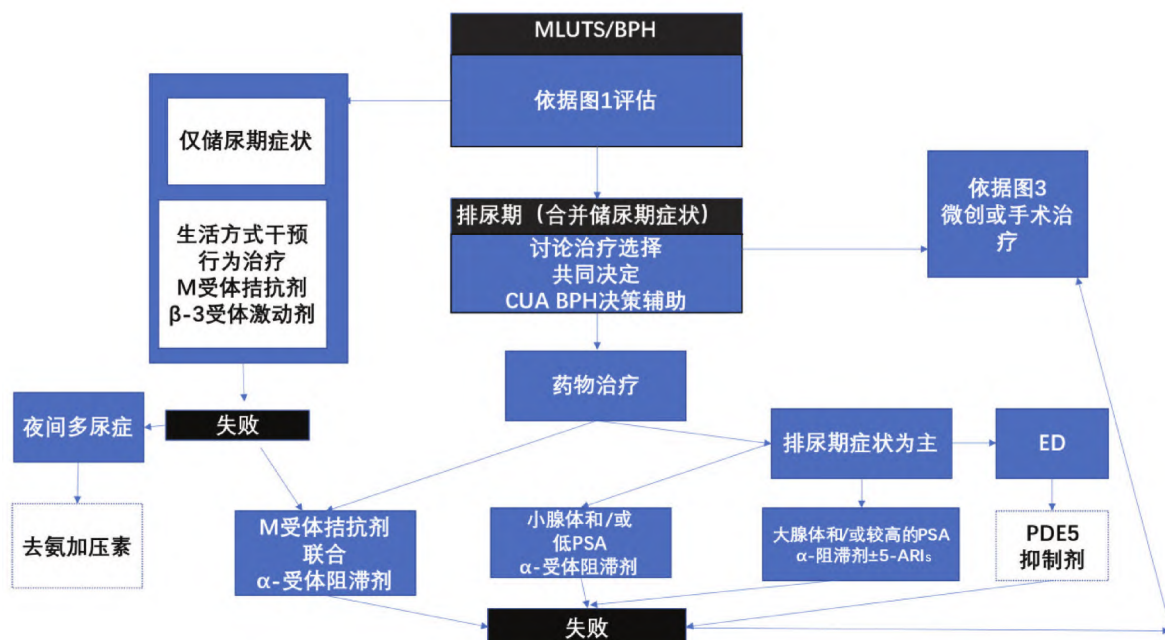


图2 男性下尿路症状/良性前列腺增生管理流程

注: MLUTS为男性下尿路症状; BPH为良性前列腺增生; ED为勃起功能障碍; PDE5为磷酸二酯酶5; PSA为前列腺特异性抗原。

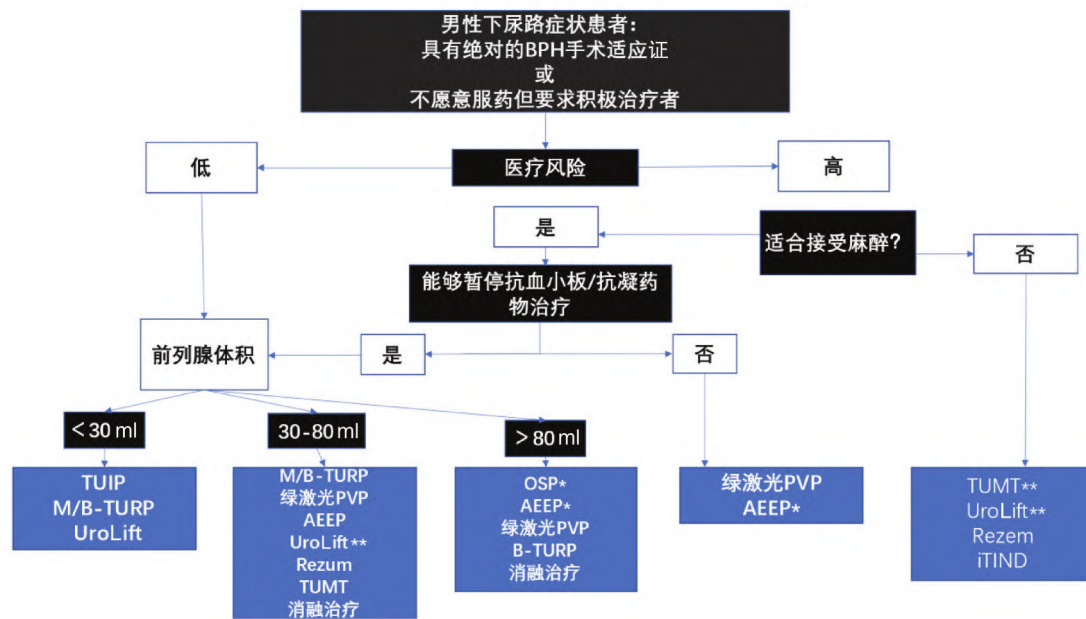


图3 对保守/药物治疗无效或具有绝对手术指征的令人烦恼的下尿路症状治疗方法流程图

注：流程图根据患者的麻醉耐受能力、心血管风险和前列腺体积进行分层。*代表现行标准/一线选择，替代疗法按字母表顺序列出。**表示必须排除前列腺中叶增生。BPH为良性前列腺增生症；B-TURP为双极等离子系统经尿道前列腺电切术；HoLEP为钬激光前列腺剜除术；iTIND为临时性镍钛装置/支架植入术；M/TURP为单极系统经尿道前列腺电切术；PVP为光选择性前列腺汽化术；TUIP为经尿道前列腺切开术；TUMT为经尿道微波治疗；AEEP为前列腺解剖内镜下剜除术；UroLift为前列腺悬扩术；TUMT为经尿道微波治疗；OSP为开放性前列腺摘除术。

别并避免可降低膀胱收缩力或增加尿道阻力的药物。可选择的治疗措施有行为改进（包括按预定时间排尿和/或重复性排尿），清洁的间歇性自我导尿，或留置导尿管^[112]。研究数据显示，DU并不一定是TURP或前列腺摘除手术的绝对禁忌证^[113-114]。“暂无针对DU管理的基于证据的具体建议。”

2.5.3 BPH相关血尿 对于BPH相关血尿，需要进行完整的评估，包括病史和体格检查，尿液分析（尿常规镜检、微生物培养、药敏、细胞学），上尿路影像学评估和膀胱镜检查是必要的，以排除其他来源的血尿。非那雄胺被报道可降低BPH相关血尿的复发风险^[115]。“建议BPH相关血尿的患者可尝试应用5-ARIs治疗（可选择性推荐，证据级别C）。”

2.5.4 不除外前列腺癌的BPH患者 对于血清PSA升高且前列腺穿刺活检阴性的BPH患者，需要指出5-ARIs治疗（非那雄胺、度他雄胺）可能会降低前列腺癌的检出率^[116-117]。患者必须认识到应用5-ARIs可能会导致高级别（Gleason 8~10）前列腺癌发病率的绝对风险值轻微增加（0.5%~0.7%）。大多数专家认为，这种现象是由于5-ARIs诱导的前列腺腺体细胞减少的假象造成的，而且似乎没有出现前列腺癌死亡率的明显增加^[118]。接受5-ARIs治疗的患者在PSA经过6~12个月达到最低点后，再出现PSA升高时，应评估高级别前列腺癌的可能性^[119]。“建议在

接受5-ARIs治疗BPH的患者中，进行病例对病例的、针对患者的知情讨论和密切的PSA随访（可选择性推荐，证据级别B）。”

3 解读

BPH诊治指南为不同医疗条件下的泌尿外科医师选择合理的前列腺增生诊断及治疗手段提供相应的临床指导，同时泌尿外科医师也应该在临床实践过程中依据患者的个体化差异进行个体化的治疗。随着循证医学证据的不断增加，BPH诊治中不断出现新的理念及治疗方法，指南的更新则对这些新的内容进行完善。我国关于BPH诊治的最新指南为2019版《中国泌尿外科和男科疾病诊断治疗指南》中前列腺增生部分，2022版CUA指南更新纳入了新的临床研究进展，比如在治疗方面新增了临时性镍钛合金植入术。指南作为临床实践指导性的文件，基本囊括了诊断、治疗的各个方面。加拿大该版指南，在诊断建议方面，仍然强调病史、查体、症状量表等重要性，与目前BPH诊治更多转向LUTS症状学的诊治是一致的；在各种仪器检查方面，则根据不同的临床需要，有选择性地进行某一项或几项检查。治疗建议方面，多种新的微创治疗手段，如经尿道前列腺微波治疗、前列腺悬扩术、前列腺水蒸气消融术、临时性镍钛合金植入术、前

列腺动脉栓塞等, 虽然不如TURP等经典手术应用广泛, 但对于一些不适合行TURP等手术且迫切需要症状改善的病例, 确实带来了治疗的希望, 这方面的临床应用数据也将不断更新。

4 总结

BPH继发的MLUTS仍然是困扰男性最常见的年龄相关疾病之一。随着人口老龄化的发展, 越来越多的男性患者将从他们的保健医那里寻求建议及针对症状的治疗指导。本指南文件中提供的信息基于对现有最佳证据的共识评估, 将有助于泌尿外科医生努力为患者提供最先进的医疗照护。

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