

经口胆胰管镜临床应用进展

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【提要】 胆胰系统疾病是消化道诊治的一大难点, 内镜逆行胰胆管造影术是胆胰系统疾病的常用诊治手段, 已广泛应用于临床, 但无法进行直视化诊治, 无法精准评估病变的程度。随着科学技术的进步, 经口胆胰管镜应运而生, 使得消化道最后一个盲区得以点亮。本文对经口胆胰管镜在胆胰系统疾病的临床诊疗中的应用进行了概述, 主要包括胆胰系统的直视下诊断和靶向活检、辅助射频消融和光动力治疗、困难胆胰管结石辅助碎石、胆囊疾病诊治等。

【关键词】 胆管疾病; 经口胆胰管镜; 内镜诊疗

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Progress in clinical application of peroral biliary-pancreaticoscopy

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经口胆胰管镜作为内镜逆行胰胆管造影术(endoscopic retrograde cholangiopancreatography, ERCP)的辅助手段于1970年首次被描述, 随着经口胆胰管镜的迭代更新及临床适用范围的扩大其越来越受欢迎。经口胆胰管镜检查可直视胆胰系统, 为诊断和治疗提供了更多可能性。随着胆胰管镜图像质量的提高, 其诊断能力也随之提升; 随着胆胰管镜耐用性和可操作性的提高, 其在治疗中的应用潜力也在增加^[1]。经口胆胰管镜外径小、成像清晰、种类齐全、配件多样, 且单人操作更加灵活, 产品主要包括SpyGlass(美国波士顿科学公司)、eyeMAX(中国南微医学科技股份有限公司)等操作系统, 可广泛应用于胆胰、阑尾等相关疾病的诊治^[2-3]。

一、胆胰系统疾病的诊治

(一)胆胰系统疾病的诊断

1. 狭窄评估及靶向活检

各种胆管病变均可引起胆管狭窄, 多达20%的胆管狭窄在常规检查及ERCP胆管取样后仍无法确定, 需要手术切除并进行病理活检才能明确诊断, 并且四分之一疑似恶性胆总管狭窄的患者在手术后被发现为良性病变^[4]。胆管狭窄的良恶性鉴别非常重要, 直接影响临床的治疗及患者预

后。经口胆管镜可以直接观察胆管并对可疑病变进行有针对性的靶向活检, 在无法获得明确诊断的情况下为鉴别胆管良恶性狭窄提供了新的手段^[5]。研究发现, 经口胆管镜直视下视觉诊断胆管病变良恶性的敏感度为90%~100%, 特异度为62.5%~95.8%, 值得注意的是, 在胆管镜检查中肿瘤血管、乳头状突起、结节或息肉样肿块以及浸润性病变是恶性胆管狭窄的重要特征^[1]。经口胆管镜与窄带光成像相结合相较于白光成像对胆管狭窄的视觉诊断质量更高^[6], 并且使用人工智能从经口胆管镜图像转换的虚拟靛胭脂染色内镜图像与窄带光成像相比, 可更好地显示出胆管表面结构和病变边缘^[7]。经口胆管镜直视下活检在区分良恶性病变方面的敏感度为63.6%~100%, 特异度为89.5%~100%^[8-11]。经口胆管镜直视下活检的敏感度有待进一步提升, 其中获取足够标本组织, 对胆道病变活检组织进行充分采集是解决这一问题的关键^[12]。Deprez等^[13]的研究发现, 与ERCP相比, 经口胆管镜在胆管狭窄诊断中的应用减少了手术次数(-31%)和费用(-13 000欧元)。

2. 胆管内乳头状肿瘤(intraductal papillary neoplasm of the bile duct, IPNB)的诊断

IPNB是一种生长缓慢的胆管肿瘤, 是胆管癌的癌前病

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变并且具有高度恶变的潜能,其特征为胆管内乳头状结节或凸起,可伴有大量黏液分泌,黏液分泌过多的患者常在乳头状结节生长的主要部位表现为胆管囊性扩张^[14]。临床表现缺乏特异性,故早期诊断困难,CT和MRI可以捕捉到乳头状隆起的主要病灶,但对于未见明确肿块,仅有大量黏液分泌所致胆管扩张的患者及评估主要病灶的表面扩散和病变进展是困难的。经口胆管镜可直接观察IPNB表面扩散和病变进展,并进行直视下活检,从而能够准确诊断^[15]。IPNB在胆管疾病中极为罕见,根治性手术治疗是目前的主要治疗方法,Luvira等^[16]报道胆管切除残端浸润性癌检测阳性,总生存率显著降低,而非典型增生和原位癌检测阳性不影响预后。因此IPNB的早诊早治十分重要,随着经口胆管镜的发展及推广应用,相信可进一步提高IPNB的早期诊断,改善患者预后。

3. 胰腺导管内乳头状黏液性肿瘤 (intraductal papillary mucinous neoplasm, IPMN) 的诊断

IPMN具有恶变倾向,发生癌变后,患者的五年生存率不足40%^[17]。影像学表现并不典型,与其他囊性病难以区分,尽管ERCP能充分显示主胰管扩张及不规则充盈缺损,但不能准确判断IPMN类型及范围。有学者提出,经口胆管镜是用于评估IPMN及主胰管扩张的有效工具,并可指导手术方式的选择^[18-20]。ERCP和经口胆管镜联合可实现IPMN的精准诊断,在镜下往往可以观察到胰管内黏液物质、绒毛状突起和丰富的血管网^[21]。

4. 肝门部胆管癌 (hilar cholangiocarcinoma, HCCA) 的术前分期

经口胆管镜可用于术前评估HCCA患者的肿瘤衍生情况,帮助外科医师决定手术可切除性和选择手术方式,影响患者预后^[22]。Pereira等^[9]的研究发现,经口胆管镜评价HCCA患者情况时,有42.1%的患者解剖分型与先前影像学定义的解剖分型不符,其中21%的患者因解剖分型改变而改变了手术方式。有研究发现术前加行经口胆管镜评估胆管黏膜及肿瘤侵犯范围可以提高肝外胆管癌R0切除率^[23]。在未来,经口胆管镜及影像学结合评估HCCA血管病变的延伸可能会优化手术方式。

5. 原发性硬化性胆管炎 (primary sclerosing cholangitis, PSC) 的评估

PSC是一种以多灶性胆管狭窄和进展期肝病为特征的少见疾病,PSC患者患胆管癌的风险显著增加^[24],因此定期监测对PSC患者十分重要。经口胆管镜的可视化诊治可能对评估PSC的狭窄及病情进展有一定的作用。Sandha等^[25]根据经口胆管镜下的图像特征为PSC开发了一种新的胆管狭窄分类方法,根据视觉特征将PSC分为三种表型,即炎症型、纤维狭窄型和结节性肿块形成型,表型可以用来评估患者患恶性肿瘤的风险,并帮助指导进一步的治疗。经口胆管镜直视下的图像特征可对PSC患者的胆管狭窄进行良性识别,使获得足够的靶向活检组织^[26]。经口胆管镜对PSC患者的病情评估是有效的,并且可能成为PSC患者长期管理的有效工具。

6. 胆道出血的评估

磁共振胰胆管成像术 (magnetic resonance cholangiopancreatography, MRCP) 及 ERCP 可以显示胆道出血,但是无法明确胆道出血的原因及来源,经口胆管镜检查直视下观察可以帮助确定胆道出血的原因^[27]。Sum等^[28]报道了1例壶腹部出血的患者经口胆管镜检查后明确为胆总管血管发育畸形的罕见出血原因。Zhang等^[29]报道了1例经口胆管镜检查证实胆囊癌继发胆囊出血并采用全覆膜自膨式金属支架治疗的病例。

(二) 胆胰系统疾病的治疗

1. 困难胆管结石的治疗

目前ERCP已经成为胆管结石的主要治疗方法,然而,有10%~15%的胆管结石患者,无法通过常规ERCP去除结石^[30]。经口胆管镜直视下碎石术的出现为此类困难结石的治疗提供了新的选择,经口胆管镜可实现直视下液电碎石或激光碎石^[31-32]。对于困难胆管结石,通过一次治疗可实现结石清除率为58%~87%,通过多次治疗可实现总计结石清除率为77%~100%,且安全有效^[33]。Deprez等^[13]在成本效益分析中发现,使用经口胆管镜治疗困难胆管结石分别减少了27%的手术次数和11%的手术成本。经口胆管镜直视下取石在减少辐射量方面显著优于传统X线下ERCP^[34]。因此,对于儿童或妊娠期胆管结石急性发作的患者,可尝试经口胆管镜辅助下无射线ERCP,以达到免射线下胆总管结石治疗的目的,然而仍需进一步的高质量前瞻性研究予以证实。

Mirizzi综合征 (Mirizzi syndrome, MS) 是指胆囊管或胆囊结石嵌顿后压迫相邻胆管导致其部分或完全堵塞而引起的一种临床并发症,根据胆囊胆管瘘的严重程度以及是否存在胆囊肠瘘将MS分为五种类型 (I、II、III、IV、V型)^[35]。ERCP提供了肝外胆管的可视化,并且可以识别外在的胆道压迫和胆囊胆管或胆囊肠瘘的存在^[36],然而由于MS特殊解剖位置及结石嵌顿,常规ERCP对于MS的治疗成功率较低。经口胆管镜具有直视下诊断及治疗的优势为MS的治疗提供了新的方法。2011年Issa等^[37]报道了第一例经口胆管镜下激光碎石治疗难治性I型MS成功的案例。经口胆管镜引导下激光碎石可实现胆囊管结石单次清除率高达94%,且术后不良反应少^[38],多次碎石后结石清除率可达100%^[39]。多例病例报告报道了经口胆管镜引导下激光碎石或液电碎石成功碎石的MS患者,为MS的治疗提供了经验^[40-43]。对于IV型MS,Soriani等^[44]报道了碎石下胆管再通并放置塑料支架引流,Li等^[45]描述了经口胆管镜引导下胆囊管碎石后再次手术切除胆囊并T管引流避免了胆肠吻合术,Kawai等^[46]则在经口胆管镜引导下液电碎石实现结石完全清除。

肝内胆管结石 (intrahepatic bile duct, IHBD) 病情复杂、病变广泛,同时术后复发率、残石率以及并发症发生率均较高^[47]。研究发现,经口胆管镜引导下肝内胆管结石的诊断率为97.14%,一次性取石成功率为85.71%,并发症发生率

为 8.57%^[48]。肝空肠吻合术后可引起 IHBD,完全清除结石和消除胆汁淤积十分必要^[49]。一项肝空肠吻合术后患者 IHBD 治疗的前瞻性研究发现,使用双球囊小肠镜联合经口胆管镜可检测到肝内胆管结石残留并去除,手术相关不良事件的发生率为 7%,且术后复发率低^[50]。对于胆总管十二指肠瘘合并 IHBD 的患者,Yamamoto 等^[51]尝试在经口胆管镜引导下对胆总管十二指肠瘘进行插管,并将导丝插入肝内胆管进行液电碎石以清除所有肝内胆管结石和碎片,患者术后恢复迅速,强调了在胆总管十二指肠瘘合并肝内胆管结石的患者中使用经口胆管镜与液电碎石的益处。

2. 困难胰管结石的治疗

胰管结石可导致主胰管狭窄继而引发胰液引流不畅、引起胰管高压,胰管结石治疗的目的是去除结石、解除梗阻,改善疼痛和预防胰腺炎的发生^[52]。较小的(长径 \leq 5 mm)胰管结石可选择 ERCP 和胰括约肌切开术,并辅以网篮或球囊取石治疗^[53],然而对于较大胰管结石的完全清除存在一定的挑战。经口胰管镜的发展为困难胰管结石的治疗提供了新的思路,经口胰管镜可显示主胰管,并使用液电和激光进行直视下碎石。经口胰管镜治疗困难胰管结石总体成功率为 85.77%~95%^[54-56],经过多次治疗后结石完全清除率达 88.9%~90%^[57-58]。经口胰管镜激光碎石具有取石成功率高、并发症发生率低的优势,但是关于经口胰管镜联合激光碎石在胰管取石中研究仍相对较少,仍需要进一步深入研究。

3. 辅助射频消融和光动力治疗

胰胆管癌是临床上常见的恶性肿瘤,手术切除是目前唯一根治性的治疗方法。由于其发病隐匿、恶性程度高,首诊时通常已处于中晚期,大多数患者往往失去了根治性手术机会,预后极差。对于失去手术机会的晚期恶性胆管狭窄患者,内镜下置入胆管支架是目前最主要的胆管引流手段,用于恢复胆汁引流通畅达到减黄、保肝作用^[59]。基于 ERCP 技术的消融治疗被认为可以提高支架通畅时长并延长患者生存时间^[60]。目前,内镜下消融治疗主要包括光动力以及射频消融这两种方式^[61]。据报道,ERCP 指导下消融治疗不良事件发生率的范围很广,从 0% 到 62% 不等^[62],严重的不良事件如手术相关死亡^[63]或胆道穿孔^[64]也有报道。经口胆管镜可用于术前评估胆管病变及定位,从而降低穿孔、出血等并发症发生风险^[65]。经口胆管镜直视下对肿瘤组织进行射频消融治疗,对控制肿瘤进展有明确作用,并可降低支架堵塞的风险,延长支架的通畅时间,临床安全可行^[66-67]。然而,有研究发现对于失去外科手术机会的胆管恶性狭窄患者,胆道镜直视下姑息性射频消融联合置入胆管支架相较于单纯胆管支架引流未显现出明确的优势,且增加了术后胆管炎的发生风险^[68]。研究发现,经口胆管镜直视下诊断+活检联合射频消融同台诊治不可切除肝外胆管癌可减少 ERCP 次数,并且不增加术后不良事件发生率,是一种安全有效且具有较高成本-效益比的诊治方法^[69]。有学者提出经口胰管镜和管腔内射频消融或光动力治疗的

组合在治疗导管内乳头状肿瘤方面似乎是一种有前途、可行、耐受性良好且安全的治疗方法,然而仍需要更多大样本、多中心、前瞻性研究来进一步评估这一结果^[70-71]。

4. 移位胆胰管支架的处理

胆管支架移位发生率为 5%~10%,可以是近端或远端支架移位,移位的支架可造成胆汁引流受阻、支架阻塞从而继发胆道感染及胆汁淤积^[72]。需要移位支架取出及对狭窄部位再次放置支架,经口胆管镜可辅助胆管内移位支架的取出。较多文献报道了在经口胆管镜直视下成功取出胆管内移位支架,并在狭窄部位再次放置支架,且术后患者恢复良好^[73-75]。其中,金属支架的放置随着时间的延长会导致复发性胆道梗阻的发生,研究发现可在经口胆管镜直视引导下采用液电碎石或导丝进行适当的再干预实现支架再通^[76-77]。

胰管相较于胆管具有内径更小、更迂曲的特点,胰管支架更易移位、支架取出更困难。经口胰管镜相较于 ERCP 具有直视下的优点,Thongpiya 等^[78]和 Rahimi 等^[79]报道了 SpyGlass 直视下联合 SpyBite 钳取出胰管支架并重新进行支架定位,为移位胰管支架的处理提供了经验。

5. 困难胆管狭窄的导丝超选

经口胆管镜可以进一步提高肝移植术后、胆囊切除术后等复杂胆管狭窄的诊疗效率,帮助确定胆管狭窄的具体位置。胆管狭窄治疗中的关键操作是导丝通过狭窄,并在此基础上进行后续操作。Bokemeyer 等^[80]研究显示,ERCP 常规方法失败的困难胆管狭窄中,经口胆管镜的成功率为 70%,其中良性狭窄的通过率明显高于恶性狭窄。对于肝移植术后困难吻合口狭窄,经口胆管镜下超选具有更高成功率^[81]。经口胆管镜直视下有助于 PSC 患者导丝穿过传统方法无法通过的胆管狭窄,且无严重并发症^[82]。

6. 急性胆囊炎的治疗

急性胆囊炎是一种肝胆外科常见的、高发的急腹症,病情变化较快,可伴有严重并发症。对于无法进行胆囊切除术或延迟手术的急性胆囊炎患者,经乳头胆管支架植入术(endoscopic transpapillary gallbladder stenting, ETGS)已作为除抗生素外的一种预防性治疗方法^[83]。然而无法胆管内插管是 X 线透视引导下 ETGS 失败的主要原因之一。经口胆管镜可直视下辅助 ETGS,可提高 X 线透视引导失败后的成功率,使 ETGS 的总体成功率从 53% 提高到 75%,在透视引导下接受 ETGS 的患者与接受经口胆管镜辅助 ETGS 的患者之间的不良事件发生率和复发率差异无统计学意义^[84]。ERCP+经口胆管镜治疗对比经皮胆管穿刺引流术+ERCP 治疗胆总管结石继发急性胆囊炎,两者的手术相关不良事件和风险及治疗效果相当,且安全有效^[85]。对于胆总管结石合并胆囊颈结石和急性胆囊炎的患者,采用 ERCP 联合经口胆管镜治疗相对安全、可行、有实用性^[86]。

7. 胆囊息肉的治疗

胆囊息肉可引起症状,并可能是癌前病变。大多数小的息肉如果没有症状,可以进行腹部超声随访。ERCP 联合

经口胆管镜能够通过自然腔道进入胆囊管、胆囊并进行胆囊息肉切除,一方面可以保留胆囊,另一方面可以减少对周围脏器的影响。王宏光团队报道了在经口胆管镜辅助下热活检钳切除小胆囊息肉且患者术后恢复良好,展示了经口胆管镜在取样和切除小胆囊息肉的新应用^[87-88]。然而,需更先进的技术和设备使此项技术更完善,并且需要开展多中心、大样本、随机对照临床研究以优化内镜治疗方案,提高内镜下胆囊息肉的治疗水平。

二、单纯性阑尾炎的治疗

超级微创是对应外科手术切除器官、解剖重建的一项技术,在保存器官和维持生存质量方面具有很强的优势,内镜下阑尾炎的治疗就是其中之一。内镜逆行阑尾炎治疗(endoscopic retrograde appendicitis treatment, ERAT)是一种治疗急性阑尾炎的新型微创技术,与腹腔镜阑尾切除术相比,ERAT的中位手术时间和中位住院时间显著降低,是治疗单纯性急性阑尾炎的技术上可行的方法^[89]。传统ERAT需在X线造影下观察阑尾腔,对患者及操作者均有辐射,儿童、妊娠患者应用受限。随着内镜技术的发展,胆管镜辅助ERAT为诊断和治疗急性单纯性阑尾炎提供了一种可行、安全有效的手术方法^[90]。研究发现,结肠镜联合胆管镜诊治单纯性阑尾炎技术成功率98.7%,临床成功率99.4%,治疗效果和安全性良好^[91]。使用胆管镜可以清楚观察阑尾腔内粪石、脓液、内壁黏膜充血水肿、腔内迂曲狭窄等情况,并进行直视下冲洗、支架植入、取石等治疗,直视也避免了X线和造影剂的使用,这对孕妇及儿童尤其重要^[92-93]。同时,对于其他不明原因的阑尾病变可在经口胆管镜引导直视下活检^[94]。有学者尝试使用胆管镜联合液电碎石对为长期便秘的老年患者去除了钙化粪便,缓解患者症状且无不良事件发生^[95]。

三、经口胆管镜的其他作用

Pérez-Cuadrado-Robles等^[96]和Gerges等^[97]应用经口胆管镜进行经皮诊断及活检,经口胆管镜总体成功率分别为95.5%和96%,特异度均为100%,视觉印象诊断总体准确率分别为77.3%和96.4%,并减少瘘管扩张时间。经口胆管镜可辅助经皮经肝胆管镜^[98]及腹腔镜^[99]进行胆管结石治疗,为胃肠道结构改变或ERCP治疗失败的胆总管结石患者提供了一个新的选择。

四、总结

经口胆管镜临床适应证在不断扩大,为胆胰疾病、阑尾疾病的诊治提供了新的思路,经口胆管镜可在直视下活检,为发现胆胰系统早期病变提供了诊断证据,也为医护人员提供了新的诊疗思路。经口胆管镜的发展,以及其配件的研发有助于疾病的临床诊疗,并提高了消化内镜的诊疗水平。目前,经口胆管镜最常用于胆总管结石治疗和不确定胆道狭窄的评估,对于经口胆管镜在其他系统的应用还需开展多中心、大样本、随机对照临床研究,以优化内镜治疗方案,并精准评估各种治疗方法对患者远期效果的影响。

利益冲突 所有作者声明不存在利益冲突

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