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· 综 述 ·

超声内镜引导下胆管引流在恶性胆管梗阻中的研究进展

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[摘要] 恶性胆管梗阻(MBO)因胆汁排泄障碍引起梗阻性黄疸,可能导致胆管炎、脓毒血症、肝衰竭等并发症,甚至危及患者生命,胆管引流是解除症状、改善患者生活质量的有效手段。目前,对于无手术机会的MBO患者,经内镜逆行胰胆管造影(ERCP)置入金属支架是姑息性治疗的一线方法。近年来,对ERCP失败的MBO,超声内镜引导下胆管引流(EUS-BD)技术逐渐被接受,认为是优于经皮经肝穿刺胆管引流术(PTBD)的替代方法。有证据表明,由经验丰富的术者操作,对于远端MBO患者,EUS-BD甚至可以作为一线治疗方法替代ERCP。本文就EUS-BD在MBO中的研究进展进行综述。

[关键词] 超声内镜; 内镜逆行胰胆管造影术; 胆管引流术; 经皮经肝穿刺胆管引流术; 恶性胆管梗阻

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Endoscopic ultrasound-guided biliary drainage in malignant biliary obstruction: research progress

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[Abstract] Malignant biliary obstruction (MBO) leads to obstructive jaundice as a result of bile excretion disorder, which may cause complications such as cholangitis, sepsis, hepatic failure and even life-threatening. Biliary drainage is an effective mean to relieve symptoms and improve patients' quality of life. At present, endoscopic retrograde cholangiopancreatography (ERCP) is the first-line palliative treatment for MBO patients without surgical opportunity. In recent years, endoscopic ultrasound-guided biliary drainage (EUS-BD) has been gradually accepted as an alternative to percutaneous transhepatic biliary drainage (PTBD) in MBO with failed ERCP. The available evidence suggests that EUS-BD might even replace ERCP as the first-line procedure in patients with malignant distal biliary obstruction by experienced surgeons. This paper reviews the research progresses of EUS-BD in MBO.

[Key words] endoscopic ultrasound; endoscopic retrograde cholangiopancreatography; biliary drainage; percutaneous transhepatic biliary drainage; malignant biliary obstruction

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恶性胆管梗阻(malignant biliary obstruction, MBO)通常是指胰腺、胆管、壶腹部、肝门部等部位的原发或转移癌引起的胆管梗阻,早期多无特异表现,随病程延长可出现腹痛、黄疸、腹部包块等症状,但此时疾病已属晚期,绝大多数丧失外科手术机会,解除胆管梗阻是改善患者生活质量的主要方法^[1]。内镜逆行胰胆管造影(endoscopic retrograde cholangiopancreatography, ERCP)因创

伤小、并发症发生率低、可重复操作等优点,是目前首选的姑息性治疗MBO的方法^[2-3]。然而,有3%~10%的患者因为壶腹部肿瘤侵犯或术后解剖结构改变等原因导致ERCP失败或无法进行ERCP^[4-5],经皮经肝穿刺胆管引流术(percutaneous transhepatic biliary drainage, PTBD)是这部分患者的替代治疗方法,但是诸如出血、胆瘘、胆管炎等并发症的发生率较高,并且受肝内胆管扩张程度的

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限制, 外接引流也极大影响了患者的生活质量^[6-8]。

超声内镜引导下胆管引流(endoscopic ultrasound-guided biliary drainage, EUS-BD)技术于2001年首次被报道, 其后超声内镜引导下胆管十二指肠吻合术(endoscopic ultrasound-guided choledochoduodenostomy, EUS-CDS)、超声内镜引导下肝胃吻合术(endoscopic ultrasound-guided hepaticogastrostomy, EUS-HGS)、超声内镜引导下对接技术(endoscopic ultrasound-guided rendezvous, EUS-RV)、超声内镜引导下逆行途径技术(endoscopic ultrasound-guided antegrade transpapillary stent placement, EUS-AG)等方法的出现使EUS-BD的安全性和有效性得到了有效验证和进一步提高。EUS-CDS和EUS-HGS是目前应用于MBO治疗的2种主要方法。

1 EUS-BD 技术

1.1 EUS-CDS EUS-CDS基本操作步骤为在十二指肠球部通过超声内镜(endoscopic ultrasound, EUS)观察到扩张的胆总管, 并在EUS引导下进行穿刺、吸取胆汁, 确认位置后注射造影剂显影胆道; 随后放置导丝, 循导丝逆行进入胆管, 然后利用探条、球囊、扩张器、针型切开刀等扩张穿刺道; 最后在胆管和十二指肠球部之间放置塑料或金属支架, 实现胆汁引流。通常胃肠道解剖正常的远端胆管梗阻患者可选择此术式。在2001年Giovannini等^[9]首次报道了此术式。一项包含16项研究528例MBO患者的meta分析显示, 该术式的总体成功率为90.9%, 并发症发生率为16.5%, 主要并发症包括胆瘘、出血、胆管炎、胰腺炎等^[10]。此外, 多项研究探讨了不同支架在EUS-CDS中的应用。Park等^[11]对32例MBO患者行EUS-BD治疗, 一组(16例)采用一步法置入改良的混合金属支架, 无穿刺道扩张, 另一组(16例)采用常规方法置入全覆膜金属支架, 2组操作及临床成功率均无明显差异, 但一步法操作时间更短(10 min vs 15 min, $P=0.007$), 且早期并发症发生率相对较低(6.3% vs 31.3%), 但差异无统计学意义($P=0.172$)。Kunda等^[12]对57例MBO患者行EUS-CDS, 利用Hot AXIOS™系统置入双蘑菇头金属支架(lumen-apposing metal stent, LAMS), 操作成功率为98.2%, 临床成功率为

94.7%, 操作相关并发症发生率为7%, 再干预防率为9.3%。El Chafic等^[13]开展的一项多中心研究发现, 随访>4周MBO患者中置入轴向定位支架和LAMS的患者再干预防率低于常规置入LAMS的患者(11.8% vs 50.0%, $P=0.02$)。以上研究结果表明, 新型支架及其系统在临床成功率方面与常规支架无明显差异, 在技术上是可行、安全、有效的。一步法可以简化操作流程, 在一定程度上减少了早期并发症, 但其长期疗效有待大样本临床试验验证。

1.2 EUS-HGS Burmester等^[14]于2003年首次报道了EUS-HGS, 其操作步骤与EUS-CDS相似, 但穿刺点为经胃壁穿刺至扩张的左肝内胆管, 操作时须注意的2个关键点: (1)应穿刺EUS显像从左上至右下的胆管, 以降低穿刺风险及导丝进入难度; (2)需有足够体积的肝实质, 以降低支架移位等并发症的发生率。EUS-HGS的适应证不限于远端胆管梗阻, 也可用于近端胆管梗阻和手术后(Whipple、Roux-en-Y术等)解剖结构改变等情况。肝胃之间存在大量腹水或胃癌晚期被认为是EUS-HGS的禁忌证。EUS-HGS的总体成功率为82%, 并发症发生率为23%, 并发症主要包括胆瘘、感染、支架功能障碍、出血等^[15-16]。肝门部胆管完全梗阻是该方法的一个重要挑战, 因为常规操作只能引流左肝内胆管, 不能引流右肝内胆管。为了克服这个局限, Ogura等^[17]对11例右肝内肝管或肝门部恶性梗阻患者进行了右肝内胆管引流, 采用双金属支架法, 其中7例用不覆膜金属支架连接左右肝管, 覆膜金属支架连接左肝管与胃, 4例用不覆膜金属支架桥接右肝管和右肝实质, 覆膜金属支架连接不覆膜金属支架末端与胃或十二指肠, 均实现了右肝内胆管的引流, 至随访结束未发现相关并发症。但该研究也强调此方法操作难度大, 应由经验丰富的内镜医师在设备完善的内镜中心进行, 以应对可能发生的各种并发症。Minaga等^[16]回顾性分析了30例肝门部恶性梗阻患者EUS-BD治疗的结果, 其中28例患者行EUS-HGS治疗, 2例行EUS-CDS治疗, 30例患者操作成功率为96.7%, 临床成功率为75.9%, 并发症发生率为33%, 操作相关并发症发生率为10%, 支架功能障碍的发生率为23.3%, 支架中位通畅时间为62.5 d, 患者中位生存期为64 d。末端裸露的覆膜金属支架相较于全覆膜金属支架可有效降低支架功

能障碍的发生率(0/13 vs 2/7),并且胆瘘等并发症发生率也较常规支架低^[18]。

1.3 EUS-RV 和 EUS-AG EUS-RV 技术于2004年被首次报道^[19],是在EUS引导下通过胃或十二指肠穿刺至扩张的胆管形成临时瘘管,然后导丝经瘘管、胆管、十二指肠乳头进入十二指肠肠腔,在该导丝的引导下行常规ERCP治疗。EUS-AG操作步骤与EUS-RV相似,不同之处在于导丝插入后支架直接沿导丝顺行放置到梗阻处。这2种方法的关键点在于导丝能否通过胆管狭窄段及十二指肠乳头,并且EUS-RV在操作过程中需要由EUS转换为十二指肠镜。EUS-RV的先决条件是十二指肠镜可以到达十二指肠乳头,但EUS-AG不受该限制。目前相关研究较少,一项多中心前瞻性研究显示EUS-RV成功率为80%,并发症发生率为15%^[20];EUS-AG多用于少数术后解剖结构改变的良性疾病^[21],或与EUS-HGS联合用于MBO^[22],总体成功率为83%,并发症发生率为10%,主要并发症包括术后胰腺炎、出血、腹膜炎等^[20-22]。

2 EUS-BD 技术之间与其他技术的对比

2.1 EUS-BD 与 PTBD Sportes等^[23]开展的一项EUS-HGS与PTBD多中心回顾性研究发现,31例MBO患者接受EUS-HGS治疗,20例MBO患者接受PTBD治疗,2组患者的中位生存期、临床成功率、并发症发生率均无明显差异,但EUS-HGS组再干预率、住院天数均明显低于PTBD组。Télliez-Ávila等^[24]的研究认为,EUS-BD在临床成功率($P=0.04$)、并发症发生率($P=0.04$)、住院费用($P=0.03$)等方面优于PTBD。一项针对EUS-BD和PTBD的meta分析显示,EUS-BD的成功率和操作相关并发症发生率均优于PTBD^[10]。但也有研究认为,EUS-BD与PTBD有相似的成功率、并发症发生率及住院费用^[25]。另一项meta分析认为,在经验丰富的内镜中心,与PTBD相比EUS-BD临床缓解率更高、并发症发生率和再干预率更低^[26]。尽管目前的研究支持EUS-BD的证据略有区别,但均认为EUS-BD优于PTBD或与PTBD相当,因此,对于ERCP失败的MBO患者来说EUS-BD可能优于PTBD。

2.2 EUS-BD 与 ERCP Paik等^[27]对125例MBO患者进行了多中心随机临床试验,其中64例接

受EUS-BD治疗(包括32例行EUS-CDS治疗、32例行EUS-HGS治疗),另61例患者接受ERCP治疗,结果显示2组操作成功率与临床成功率均无明显差异,EUS-BD组术后并发症发生率、术后胰腺炎发生率、再干预率、6个月内支架通畅率等均优于ERCP组(6.3% vs 19.7%, $P=0.03$; 0 vs 14.8%, $P=0.001$; 15.6% vs 42.6%, $P=0.001$; 85.1% vs 48.9%, $P=0.001$),并且在术后12周EUS-BD组患者有更好的生活质量。Logiudice等^[28]对3项针对EUS-BD和ERCP的随机对照试验^[27,29-30]进行meta分析发现,在远端MBO患者中,由经验丰富的术者操作,EUS-BD显示出与ERCP相似的操作成功率、临床成功率、并发症发生率和支架通畅率,但EUS-BD在支架功能障碍方面优于ERCP,表明在经验丰富的内镜中心EUS-BD可能成为远端MBO患者的一线治疗方法。

2.3 EUS-CDS 与 EUS-HGS Uemura等^[31]对10项研究共434例ERCP失败MBO患者进行的meta分析发现,EUS-CDS与EUS-HGS的操作成功率和临床成功率无明显差异,胆管炎、出血、气腹、支架移位、腹膜炎等并发症的发生率均无明显差异,建议可以根据患者胃肠道解剖结构或梗阻部位选择合适的手术方式。Minaga等^[32]对47例MBO患者进行了前瞻性对照研究,结果显示EUS-CDS和EUS-HGS2种方法的成功率和并发症发生率无明显差异,EUS-CDS组并发症包括胆管炎2例、支架阻塞1例、支架移位1例,EUS-HGS组并发症包括腹膜炎1例、胰腺炎1例、支架阻塞4例。该研究认为在ERCP失败的MBO患者中,EUS-CDS与EUS-HGS在操作成功率、并发症发生率、支架通畅率、生存期等方面均无明显差异,提示在穿刺前做好超声评估,如果其中一种方法难度较大可选择另一种方法。也有研究认为,EUS-CDS的并发症发生率低于EUS-HGS(20% vs 29%, $P=0.01$),是一种更安全的EUS引导下引流方式^[33]。

3 小结

对于无外科手术机会的MBO患者选择何种引流方式,适应证的把握及技术的熟练程度是关键,目前ERCP仍然是首选。在经验丰富的内镜中心,对于ERCP失败的MBO患者EUS-BD可能优于PTBD,EUS-CDS与EUS-HGS之间并没有明显差

异。对于单一引流方式没有效果的MBO患者,可以采取多种联合方法,近期有研究发现ERCP联合EUS-BD治疗近端MBO取得了较好的效果^[34]。随着各种新方法、支架及系统的出现,EUS-BD展现了良好的应用前景,但它仍是有创操作,可能存在胆汁性腹膜炎、胆瘘、出血、胆管炎、支架功能障碍等并发症,并且其操作相对复杂、学习曲线长^[10]。因此,EUS-BD的安全性和有效性还需大样本临床研究验证。

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