

•论著•

ERCP在原发性肝癌围术期胆道并发症诊治中的应用

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[摘要] 目的：回顾本中心应用经内镜逆行胰胆管造影术(endoscopic retrograde cholangio-pancreatography, ERCP)在原发性肝癌围术期胆道并发症临床诊治中的经验。方法：回顾性分析2016年10月至2023年6月我院原发性肝癌诊治过程中围术期因胆道并发症行ERCP治疗病人的临床资料。依据胆道并发症行ERCP的指征，病例分为胆管癌栓组、胆管狭窄组和胆漏组。统计分析原发性肝癌围术期不同类型胆道并发症病人的基线资料、ERCP治疗前后的实验室指标、治疗转归等数据。结果：总计25例行25例次ERCP，其中23例插管成功，成功率92.0%。胆管狭窄14例次，主要行胆道球囊扩张、探条扩张、支架植入、鼻胆管引流治疗；胆漏6例次，主要行支架植入、鼻胆管引流治疗；胆管癌栓5例次，主要行网篮及气囊取栓、支架植入、鼻胆管引流治疗。ERCP治疗后病人血清总胆红素、血清直接胆红素、 γ -谷氨酰转移酶较治疗前明显下降($P<0.05$)。术后平均血淀粉酶(85.0±69.4)(21~306)U/L。所有病例均无出血、消化道穿孔、胰腺炎及其他ERCP相关并发症发生。结论：原发性肝癌围术期胆道并发症以胆管狭窄最为常见。对于有胆道并发症的原发性肝癌围术期病人，行ERCP治疗安全、有效。

关键词：内镜逆行胰胆管造影术； 原发性肝癌； 围术期； 胆道并发症

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Application of ERCP in diagnosis and treatment of biliary complications during perioperative period of primary liver cancer

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[Abstract] **Objective:** To review the experience of using endoscopic retrograde cholangio-pancreatography (ERCP) in the clinical diagnosis and treatment of biliary complications during perioperative period of primary liver cancer at our hospital. **Methods:** A retrospective analysis was conducted on the clinical data of patients undergoing ERCP treatment for biliary complications during perioperative period of primary liver cancer at our hospital from October 2016 to June 2023. According to the indications of ERCP for biliary complications, the cases were divided into bile duct tumor thrombus group, bile duct stricture group, and bile leakage group. The baseline data, laboratory test results before and after ERCP treatment, treatment outcomes, and other datas of the patients with different types of biliary complication were statistically analyzed. **Results:** A total of 25 patients underwent 25 cases of ERCP, among which 23 patients were successfully cannulated, with a success rate of 92.0%. There were 14 cases of bile duct stenosis, mainly treated with biliary balloon dilation, probe dilation, stent implantation, and nasobiliary drainage; 6 cases of bile leakage, mainly treated with stent implantation and nasobiliary drainage; 5 cases of bile duct tumor thrombus, mainly treated with net basket and balloon thrombectomy, stent implantation, and nasobiliary drainage. After ERCP treatment, the patient's serum total bilirubin, serum direct bilirubin, and γ -glutamyl transferase significantly decreased compared to those before the treatment ($P<0.05$). The postoperative average amylase was (85.0±69.4)(21~306) U/L. No bleeding, gastrointestinal perforation, pancreatitis, or other ERCP-related complications occurred in all cases. **Conclusions:** Bile duct stricture is the most common biliary complication during the perioperative period of primary liver cancer. For these patients with biliary complications during perioperative period of primary liver cancer ERCP treatment is safe and effective.

Key words: Endoscopic retrograde cholangio - pancreatography; Primary liver cancer; Perioperative period; Biliary complication

肝癌是常见的恶性肿瘤之一。虽然目前已有多种治疗方法如消融、介入和放射治疗等,但手术仍是治疗肝癌的重要手段。对于手术可切除的肝癌病例,围术期胆道并发症对肝切除术及预后造成影响。寻求有效治疗方法、积极处理肝癌术前胆道梗阻及术后胆道并发症成为亟待解决的问题^[1-4]。

肝癌围术期胆道并发症以胆管狭窄和胆漏常见,文献报道胆管狭窄发生率为2%~12%,胆漏发生率为2.6%~25%,胆管癌栓则相对少见^[5]。胆道并发症的常用治疗方法,包括内镜逆行胰胆管造影术(endoscopic retrograde cholangio-pancreatography, ERCP)、经皮经肝胆管穿刺引流术(percuteaneous transhepatic cholangiodrainage, PTCD)及外科手术。ERCP因创伤小、恢复快、并发症发生少的优点,在胆管疾病的诊治中得到广泛应用^[6]。该技术在肝癌围术期的应用还处于探索阶段,目前国内、外的相关报道仍然较少。本研究对本中心行ERCP治疗肝癌围术期胆道并发症的病例进行回顾性分析,探讨其疗效和安全性,旨在为临床应用提供更多参考。

1 资料与方法

1.1 研究对象

纳入2016年10月至2023年6月我院肝胆外科收治的原发性肝癌合并胆道并发症而围术期行ERCP治疗的病人25例,共计25例次ERCP操作,其中男性22例次,女性3例次。年龄35~71岁。原发病为肝细胞癌22例,胆管细胞癌3例。肝癌术前行ERCP指征如下:肝管狭窄(8例),胆管癌栓(5例);肝癌术后行ERCP指征如下:术后胆道狭窄(6例)、胆漏(6例)。

纳入标准:年龄≥18周岁;肝癌术前7 d至术后14 d出现腹痛、黄疸、发热等胆道梗阻或胆道感染的症状;术后引流见胆汁;实验室检查、影像学检查结果提示有胆管狭窄、胆漏、胆管癌栓;病史、实验室检查、影像学检查及ERCP操作记录完整。排除标准:不符合上述标准;肝癌术后远期出现胆道合并症;单纯诊断性ERCP检查而未予ERCP治疗病例。

1.2 ERCP操作

所有ERCP操作均由一位有超过10 000例操作经验的外科内镜专家实施。在ERCP治疗前至少完成1项包括腹部超声、腹部CT、磁共振胰胆管

成像(magnetic resonance cholangiopancreatography, MRCP)在内的腹部影像学检查评估胆道系统。麻醉方式为表面麻醉20例次,全身麻醉5例次。插管成功后,常规行胆道造影,根据病例术中实际情况行内镜括约肌切开术(endoscopic sphincterotomy, EST)或内镜十二指肠乳头球囊扩张术(endoscopic papillary balloon dilation, EPBD)。后续依据ERCP造影结果及病史检查资料决定相应内镜治疗操作方式。胆管狭窄,行球囊扩张或探条扩张,后续植入支架,支架选择依据胆管术中情况。胆漏,行内镜鼻胆管引流术(endoscopic nasobiliary drainage, ENBD)或支架植入覆盖。胆管癌栓,用取石网篮或取石球囊清理胆管取出癌栓,依据术中情况留置ENBD或植入支架。术后第1日常规检测血常规、肝功能和血淀粉酶。血淀粉酶不超过参考值3倍,则开放流质或半流质饮食;血淀粉酶超过参考值3倍则予以禁食,隔天复查淀粉酶指标。

1.3 观察指标

临床观察指标如下:临床症状、ERCP治疗经过、ERCP相关并发症等。ERCP操作成功标准如下:插管成功,胆管狭窄扩张成功,ENBD通畅,胆管支架植入到位,取栓成功。临床疗效评价指标如下:胆道梗阻解除、胆漏愈合,血清总胆红素、血清直接胆红素、碱性磷酸酶、γ-谷氨酰转移酶等水平下降,临床症状及腹部体征好转。

1.4 统计学分析

使用SPSS 26.0统计软件进行分析。计量资料以平均数±标准差表示,采用Kruskal Wallis H检验进行组间比较。计数资料以率或百分比表示,采用卡方检验或Fisher精确检验。 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 一般资料

25例次ERCP中23例插管成功,插管成功率92%,经ERCP治疗后获得确切临床疗效。肝癌围术期胆道并发症包括术前肝管狭窄8例、胆管癌栓5例,术后胆道狭窄6例,术后胆漏6例。主要临床症状为腹痛9例,黄疸25例,发热14例,引流胆汁6例。不同胆道并发症组间性别、年龄、肝癌病因差异无统计学意义。不同胆道并发症组的临床症状除腹痛、黄疸外,差异均有统计学意义。胆管狭窄及胆漏的发热症状较癌栓组多($P=0.004$),胆漏的

表 1 原发性肝癌围术期胆道并发症的 ERCP 治疗资料 ($\bar{x} \pm s/n$)Tab 1 Clinical data of ERCP treatment of perioperative biliary complications in primary liver cancer ($\bar{x} \pm s/n$)

Clinical features	Total (n=25)	Biliary stricture (n=14)	Bile leakage (n=6)	Bile duct tumor thrombus (n=5)	Statistical Value	P Value
Gender					$\chi^2=0.875$	0.646
Male	22	12	5	5		
Female	3	2	1	0		
Age (years)	55.0±9.5	53.8±11.0	58.6±8.2	53.2±9.6	F=0.570	0.574
Causes of liver cancer					$\chi^2=2.442$	0.295
Hepatitis B	18	9	4	5		
Other	7	5	2	0		
Clinical symptom						
Abdominal pain	9	7	2	0	$\chi^2=4.022$	0.134
Jaundice	25	14	6	5	-	-
Fever	14	8	6	0	$\chi^2=11.085$	0.004
Bile drainage	6	0	6	0	$\chi^2=25$	< 0.001
Asymptomatic	0	0	0	0	-	-
ERCP procedure						
ENBD	6	2	1	3	$\chi^2=4.454$	0.108
Stent implantation	19	12	5	2	$\chi^2=4.454$	0.108
Balloon/probe dilation	4	3	1	0	$\chi^2=1.261$	0.532
Thrombus removal	5	0	0	5	$\chi^2=25$	< 0.001
Postoperative amylase(U/L)	85.0±69.4	96.3±83.0	81.0±57.7	58.0±20.6	F=0.563	0.578

症状中引流管见胆汁较胆管狭窄及癌栓组明显($P < 0.001$)(见表1)。

2.2 ERCP治疗

胆管狭窄组共 14 例次 ERCP 操作。其中 12 例次植入支架,占比 85.7%;3 例次行胆管扩张,占比 21.4%;2 例次留置 ENBD,占比 14.3%;1 例次因导丝插入胆管后反复尝试无法通过狭窄段,后续行 PTCD 治疗。胆漏组共 6 例次 ERCP 操作。其中 5 例次植入支架、占比 83.3%;1 例次行胆管扩张,1 例次留置 ENBD。胆管癌栓组共 5 例次操作,均行网篮或球囊取栓操作。2 例次植入胆管支架,3 例次留置 ENBD。不同胆道并发症分组的 ERCP 治疗操作除胆道取栓外,ENBD、支架植入及扩张操作,组间差异均无统计学意义。ERCP 治疗后病人肝功能指标除碱性磷酸酶外,血清总胆红素、血清直接胆红素、 γ -谷氨酰转移酶较治疗前明显下降,差异有统计学意义($P < 0.05$)(见表2)。术后平均血淀粉酶(85 ± 69)(21~306) U/L,所有病例均无出血、消化道穿孔、胰腺炎等 ERCP 相关并发症发生。

3 讨论

本研究发现肝癌围术期胆道并发症主要包括

胆管狭窄、胆漏及胆管癌栓,以胆管狭窄和胆漏常见。

表 2 ERCP 治疗肝癌围术期胆道并发症前、后肝功能情况 ($\bar{x} \pm s$)Tab 2 Liver function status before and after ERCP treatment of perioperative biliary complications in primary liver cancer ($\bar{x} \pm s$)

Liver function test item	Pre-ERCP	Post-ERCP	t Value	P Value
Total bilirubin ($\mu\text{mol/L}$)	98.281±45.720	34.900±12.576	7.317	< 0.001
Direct bilirubin ($\mu\text{mol/L}$)	60.147±30.481	20.211±7.753	6.580	< 0.001
Alkaline phosphatase (U/L)	167.321±83.124	148.046±56.851	0.985	0.334
γ -Glutamyl transferase (U/L)	68.084±30.872	52.286±21.364	2.761	0.011

胆管狭窄的临床症状以黄疸、发热症状为主。肝癌围术期胆管狭窄根据其出现的时机不同,分术前与术后两类。研究表明,肝癌术前合并胆管狭窄的病例占肝癌总体的 4%~23%^[7]。肝癌合并胆管狭窄的主要原因是肿瘤侵犯胆管引起梗阻或压迫肝门胆管^[8]。对于肝癌合并胆管狭窄,主要通过血清学检查以及 CT、MRI 等影像学检查进行诊断^[9]。

ERCP及经皮穿刺胆道造影可明确狭窄部位,还能用于治疗^[10]。本研究应用ERCP针对肝癌合并胆道狭窄进行术前减黄,肝功能改善明显,肝脏手术均顺利完成,ENBD及支架植入病例行肝切除手术后均未出现胆道并发症。近期研究显示,肝癌术后胆管狭窄的发生率为5%~15%,常见的风险因素有肝切除范围大、年龄大、合并症(如糖尿病、高血压等)、术前黄疸等^[11-12]。肝切除术后胆管狭窄的治疗手段有多种,其中常用的是经皮胆道扩张术和ERCP^[13]。如内镜或经皮治疗失败,可能需再次手术^[14]。本研究所有胆道狭窄病人经ERCP治疗后,无需再次手术,仅有1例因导丝插入胆管后反复尝试无法通过狭窄段,后续行PTCD治疗,获得治愈。

肝癌肝切除术后胆漏的发生率1.5%~5%^[15]。围术期胆漏的风险因素主要涉及手术和病人两方面。手术相关风险因素包括术中损伤胆管、结扎或缝合不佳等^[16];病人相关风险因素包括年龄、性别、肝硬化、术前黄疸、糖尿病等^[17]。肝切除术后胆漏依据国际肝胆外科学会发布的国际胆道并发症分级系统进行诊断与评估^[18]。对于轻度胆漏,可利用胆管支架或胆管引流,降低胆道压力^[19];对于中度胆漏,可行ERCP治疗,植入胆管支架来达到密封效果^[20];对于无法通过保守治疗或内镜治疗控制的胆漏,需考虑再次手术^[21]。本研究所有胆漏病人经ERCP治疗后,均无需再次手术。

肝癌围术期合并胆管癌栓的病例相对较少。研究显示,原发性肝癌病例中,合并胆管癌栓者占1.2%~1.5%^[22-23]。一项2002—2008年国内的回顾性研究报道了20例肝癌合并胆管癌栓的病人^[24]。影像学检查如CT、MRI等可显示肝癌及胆管扩张情况,但单纯影像学检查往往难以明确病灶性质。从治疗方法上看,除手术切除肝癌外,还需解决胆道梗阻问题。当胆道梗阻影响肝功能时,术前取栓是一种行之有效的方法。通过ERCP、PTCD等既可以获取组织病理结果^[25],同时有助于解除梗阻。选择具体取栓方法时,应考虑病人的一般情况及病灶部位等因素。当受累部位在肝内或近肝门时,PTCD可能是更合适的选择^[26]。本研究癌栓位于肝总管及胆总管,ERCP取栓在缓解胆道梗阻、改善黄疸方面取得明确效果。值得注意的是,对于肝癌合并胆管癌栓的病人,单纯取栓治疗不能完全消除肿瘤,仍需结合术后放疗、系统治疗等辅助手段提高局部肿瘤控制率,延长病人生存期^[27]。

本研究不同胆道并发症分组的ERCP治疗操

作除胆道取栓外,ENBD、支架植入及扩张操作,组间差异均无统计学意义。对于术前胆管狭窄的病例,胆管支架植入可暂时维持胆管通畅,从而缓解梗阻性黄疸带来的肝功能异常,为肝脏手术作好术前准备。此外,术前胆道支架植入有助于降低肝癌围术期胆道并发症的发生,从而改善病人的临床预后。本研究术前植入胆管支架的病例,肝切除术后均未出现胆道并发症。对于胆漏的病例,本研究通过ERCP在胆管内植入支架,以稳定胆管结构,覆盖胆漏位置,同时有助于减轻狭窄或梗阻并改善胆汁流向。所有胆漏病例均无需再次手术。既往多项研究评估胆道支架治疗胆漏的有效性和安全性,大部分病人在支架植入后未出现严重并发症,有力地证明了ERCP胆管支架植入在治疗胆漏方面的确切疗效^[28-29]。胆管癌栓,在肝切除术前主要通过取石球囊或网篮取栓。当合并狭窄时,需同时进行胆道扩张和支架植入或引流。

肝细胞癌作为原发于肝实质内的病灶,对胆道系统的直接影响主要通过以下几种方式:形成癌栓、胆道出血、直接压迫和弥漫性肿瘤浸润。对胆道系统的间接影响主要是分泌生长因子、炎症因子等刺激胆管上皮细胞增殖或加剧胆管损伤等^[10,30]。

本研究的局限性如下:临床实践中仅有1%~12%的肝癌累及胆总管及I~III级胆管,通过ERCP处理胆总管及I~III级胆管的梗阻、狭窄、胆漏等病变有助于获得满意的临床疗效;但对于肝癌合并III级以上肝内胆管相关并发症,ERCP难以解决,治疗效果有限^[30]。此外,伴随着经口胆道子镜光纤直视系统等基于现有ERCP技术平台的新型硬件及相关技术的发展,在原有胆道造影的基础上进一步直视操作,将有助于针对癌栓、胆漏等并发症的个体化、精准化处理。

综上所述,本研究结果显示,原发性肝癌围术期常见胆道并发症有胆管狭窄、胆漏、胆管癌栓,ERCP对其具有临床价值且治疗过程安全、有效。

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·简讯·

《胃肠病学》杂志征订启事

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