

## 吲哚菁绿荧光成像技术在胆道外科的应用进展

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**【摘要】**吲哚菁绿(ICG)荧光成像技术在胆道外科的临床应用逐渐凸显其作用。ICG荧光胆道成像在腹腔镜胆囊切除术、腹腔镜胆总管探查再次手术和肝胆管结石、肝内胆管癌、肝门部胆管癌、胆囊癌等胆道外科疾病行肝切除术,以及淋巴结清扫手术、肝移植术和防治胆管损伤、胆漏等方面均具有积极作用。本文主要阐述ICG荧光成像在上述胆道外科的应用进展。

**【关键词】**吲哚菁绿;胆道外科;胆道显像;综述

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## Advances in the application of indocyanine green fluorescence imaging technique in biliary surgery

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**Abstract:** Indocyanine green (ICG) fluorescence imaging technology has gradually highlighted its role in biliary surgery. Nowadays, the technique has been used in laparoscopic cholecystectomy, laparoscopic common bile duct re-exploration, hepatectomy for biliary tract diseases such as hepatolithiasis, intrahepatic cholangiocarcinoma, hilar cholangiocarcinoma and gallbladder carcinoma, lymph node dissection, and liver transplantation. It also plays a significant role in the prevention and treatment of bile duct injury and biliary leakage. Herein the advances in ICG fluorescence imaging research in biliary surgery are reviewed.

**Keywords:** indocyanine green; biliary surgery; biliary imaging; review

### 前言

胆道外科疾病是我国常见疾病,肝胆管结石和胆道恶性肿瘤(肝内胆管癌、肝门部胆管癌、胆囊癌)等大多需要肝切除外科手术治疗才有望获得较好的疗效。日本学者率先将吲哚菁绿(Indocyanine Green, ICG)荧光成像技术应用于肝切除术,实时识别肝肿瘤和肝段边界<sup>[1-2]</sup>。目前,ICG荧光成像技术主要应用于界定肝切除范围、识别肝肿瘤边界和微小病灶<sup>[3]</sup>,但ICG荧光成像技术应用于胆道外科较少见<sup>[4]</sup>。有研究显示术中直接经胆囊或胆管推注ICG可获得较清晰的胆道成像<sup>[5]</sup>。ICG荧光成像技术在胆道外科,如腹腔镜胆囊切除术(Laparoscopic Cholecystectomy, LC)、腹腔镜胆总管再

次探查术、肝胆管结石和肝内胆管癌、胆囊腺癌、肝门部胆管癌等行肝切除术、肝移植手术或胆道恶性肿瘤淋巴结清扫、预防胆道损伤和胆漏等方面均具有积极作用。

### 1 ICG荧光成像技术基本原理和ICG荧光在胆道成像模式

ICG是一种荧光染料,在一定条件下被激发并发射近红外荧光,可被ICG荧光显像设备接收并成像<sup>[6]</sup>。ICG经胆道排泄并经ICG荧光显像设备获得胆道成像。根据ICG注射途径不同,ICG胆道成像模式有两种<sup>[7]</sup>:(1)胆道直接注射ICG胆道荧光成像。通过胆道内直接注射ICG获得胆道成像显影,用灭菌注射用水稀释至2.5 g/L,取5~10 mL,直接经肝内、外胆道或胆囊管注射可产生即时性荧光<sup>[7]</sup>。(2)静脉注射ICG胆道荧光成像。ICG经静脉注射入血后,经门静脉系统进入肝脏并经胆道排泄,在激发光照射下获得胆道荧光成像<sup>[8]</sup>。术前经外周或中心静脉注射是荧光胆道成像较常用方法,操作相对简便,

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ICG用灭菌注射用水稀释至2.5 g/L后进行注射后获得胆道成像。有研究显示手术前10~180 min进行静脉注射,剂量使用0.02~0.25 mg/kg,结果显示随着药物剂量、给药时间的递增,胆总管与肝脏的荧光强度比也逐步增加,在术前180 min、给药剂量选择为0.25 mg/kg时效果最佳<sup>[9]</sup>。目前ICG临床常用剂量为0.1~0.5 mg/kg,剂量超过0.5 mg/kg时则副反应发生率增加<sup>[10]</sup>。ICG在血液中的半衰期为2.5~3.0 min,成人和12~17岁年龄患者的最大推荐剂量是2 mg/kg<sup>[11]</sup>。索晓鹏等<sup>[12]</sup>研究报道ICG经静脉注射胆道显像,相比传统X线胆道造影,具有安全、不损伤胆道、无放射性等特点。国内的ICG共识/指南指出,ICG的剂量选择、使用方式和用药时间可根据不同的目的设置<sup>[6,13]</sup>。另外,ICG荧光胆道成像导航的即时性显像的稳定性需进一步探讨<sup>[14]</sup>。

## 2 ICG荧光成像技术在显示胆道解剖结构的价值

Daskalaki等<sup>[15]</sup>研究显示:99%的病例(184案例)在ICG荧光胆道成像中可以发现至少1个胆管结构,胆囊管、胆总管和肝总管成功显影率分别为97.8%、96.1%和94%,并发症发生率为3.2%。有文献报道该技术是安全、有效的<sup>[16]</sup>。国内学者在LC中使用ICG荧光使得胆囊管、胆总管和肝总管分别获96%、98%和98%的胆道可视化率<sup>[17]</sup>。Pesce等<sup>[18]</sup>研究显示在解剖显示胆囊三角后,肝外胆管显示率显著提升。应用ICG荧光成像技术能够在术中更快、准确地识别胆道解剖结构<sup>[19-20]</sup>。对于存在胆管变异、炎症较重的胆管辨认不清、常规手术中无法确认是否存在胆漏时,可以通过ICG荧光胆道显像发现胆漏位置,并且还可确认胆管走形、降低术中胆道损伤的风险<sup>[13]</sup>。在先天变异的胆道结构识别中,荧光胆道成像技术能够快速、准确地辨别这些异常胆道解剖结构<sup>[21-22]</sup>。该技术可以使80%的病人获得胆道显影成像,相较于普通的X线胆道造影,更具有前景<sup>[23]</sup>。

## 3 ICG荧光成像技术在LC的价值

LC是胆囊结石外科治疗的标准手术。Ishizawa等<sup>[24]</sup>首先报道了通过静脉注射ICG在LC获得胆道荧光成像。LC中胆道损伤的发生率为0.2%~1.5%<sup>[25-26]</sup>。准确辨认肝外胆道解剖结构,尤其对粘连较重、可能解剖变异的LC具有非常重要的价值。该技术在动物模型和临床环境中均被证实安全有效<sup>[27-28]</sup>,其在LC中识别肝外胆道具有可行性,且是安全和可靠的<sup>[15,28-30]</sup>。有研究显示在43例LC中采用ICG荧光成像技术有助于术者识别calot三角,提高手术的安全性<sup>[31]</sup>。ICG在LC中可以增加其安全性,减少术中放射胆道造影<sup>[32]</sup>。国内有研究显示术中通过切换白光或ICG荧光模式,白光模式

下有助于观察有无出血,ICG荧光模式下可更好地发现胆漏,进而可获得肝外胆道的可视化<sup>[14]</sup>。ICG荧光胆道成像,相对安全和稳定的肝外胆管可视化,可满足绝大多数情况下LC术中肝外胆管结构显示需求,可降低LC的手术难度,减少胆道损伤潜在风险,提高LC安全性。LC中ICG荧光成像技术有助于主刀医生更好地辨认肝外胆道解剖结构,特别对行LC手术例数尚较少的年轻医生,ICG引导手术帮助更大,有助于减少胆道损伤发生<sup>[26]</sup>。

## 4 ICG荧光成像技术在肝胆管结石及精准肝切除术的临床价值

ICG荧光成像在复杂肝胆道结石手术,可实时获得胆道成像,减少手术时间,避免胆道损伤风险。在肝胆管结石的外科治疗中,ICG荧光成像技术可实时调整肝切除手术平面,从而实现对病变区段的精准肝段切除<sup>[33]</sup>,即ICG荧光技术为精准肝切除起到实时导航目的。Inoue等<sup>[34]</sup>发现:相对于美兰染色等传统的肝段识别方式,ICG荧光成像技术更稳定、持久、界限清晰。王晓颖等<sup>[35]</sup>通过3D技术联合ICG成像技术对门静脉目标属支穿刺注射ICG实现“拼图式”精准肝段成像,完成S<sub>2</sub>~S<sub>7</sub>段的解剖性肝切除术。Sakoda等<sup>[36]</sup>经超声引导门静脉穿刺ICG荧光成像,获得了腹腔镜解剖性亚肝段肝切除术的成功。在44例随机对照研究中,研究组采用ICG外周静脉成像方法辅助开腹和腹腔镜肝切除术与传统的肝切除术进行肝胆管结石治疗,结果显示ICG组失血量较少、住院时间较短,以及术后炎症指标白细胞、降钙素原等优于传统组<sup>[37]</sup>。临床应用中,ICG荧光成像技术有助于精准的解剖性肝切除术。

## 5 ICG荧光成像技术在再次胆道手术的应用价值

如何正确辨认肝内外胆道系统和避免胆道误伤是胆道外科医生必需面对的问题。再次腹腔镜胆总管探查手术由于腹腔粘连、胆道解剖结构改变等,使得胆管的寻找和确认非常困难,增加了腹腔镜胆总管探查手术的难度<sup>[38]</sup>。ICG荧光胆道成像技术可实时可视化肝外胆道结构,帮助定位胆管<sup>[24]</sup>。有研究采用ICG技术在30例病人腹腔镜胆总管探查手术可获得胆管结构可视化,提高了手术安全性和减少并发症<sup>[39]</sup>。

## 6 ICG荧光成像技术在胆道恶性肿瘤的应用价值

胆道恶性肿瘤是肝胆外科较难治疗且预后较差的疾病之一。如肝内胆管癌具有较强的浸润性生长和肝内转移等特性,病情进展快,预后较差<sup>[40]</sup>;但肝内胆管癌外科治疗如获得R<sub>0</sub>切除,可提高远期生存率<sup>[41]</sup>。

Yang等<sup>[42]</sup>研究显示:对符合研究标准的16例肝内胆管细胞癌病人采用一种新的ICG荧光成像技术(基于胆道梗阻区域ICG滞留致胆道梗阻区域肝段染色),即通过手术前12~24 h外周静脉注射ICG,正常肝脏组织中的ICG通过胆道系统排泄(清除),而ICG在胆道梗阻区域仍滞留而使得胆道梗阻/病灶肝段染色,基于此技术特点对伴有胆道梗阻的肝内胆管癌进行引导肝切除术,可获93.8%(15/16)的清晰准确的肝切除边界,说明该技术安全、有效、可行,给伴有胆道梗阻的肝内胆管细胞癌提供了一种安全、可选择的外科治疗策略。在肝内胆管癌外科治疗中,ICG荧光成像技术可用于导航解剖性肝切除术<sup>[43]</sup>、准确界定癌灶边界和肝切除范围、检测胆漏等<sup>[44-45]</sup>。曾宁等<sup>[46]</sup>对3例肝门部胆管癌病人采用ICG荧光成像联合增强现实技术进行肝门部胆管肝切除术手术,初步结果显示安全可行。ICG荧光示踪引导腹腔镜肝内胆管癌手术中淋巴结廓清的研究显示,ICG成像组在获得淋巴结枚数、确诊病理阳性率均高于传统对照组<sup>[47]</sup>。胆囊癌是一种预后较差的胆道恶性肿瘤,根治性外科治疗通常需要进行肝外胆管周围广泛的切除和/或肝切除术。有研究采用ICG成像技术导航机器人根治性切除胆囊腺癌,结果显示10例病人手术顺利完成并获得阴性切缘,术后30 d无死亡和重大并发症,说明ICG成像技术有助于胆囊癌获得胆管阴性切缘,且有利于肝外胆管周围淋巴廓清<sup>[48]</sup>。ICG荧光成像联合3D对肝门部胆管癌进行术前准确评估,可减少手术时间和并发症<sup>[49]</sup>。将ICG荧光成像与3D技术<sup>[50]</sup>、3D流域分析、3D残肝体积分析<sup>[51]</sup>、术中超声技术等灵活运用,制定合理的手术方案,进而让ICG荧光成像发挥更大作用。

## 7 ICG在肝移植的应用价值

在活体供肝移植中,ICG荧光胆道成像技术可以帮助确定最佳的胆道分离点,优化供肝和受体的安全性;同时,该技术可帮助获得清晰的胆道图像,为判断供体肝切除术中的胆道切除提供准确位置,减少胆漏、胆管狭窄的发生<sup>[52-53]</sup>。李宏宇等<sup>[54]</sup>在小儿活体肝移植腹腔镜解剖性肝段获取中,通过利用ICG荧光技术可较好地识别肝脏S<sub>2</sub>段和S<sub>3</sub>段胆道位置和走行,从而保护肝S<sub>2</sub>段胆道免受误伤。采用ICG荧光成像技术导航腹腔镜解剖性肝段获取术,术中可实时、完美地显示肝段与肝段界限<sup>[55]</sup>。有报道采用ICG清除试验判断原位肝移植术后1年内缺血性胆道病变发现:在无肝动脉血栓形成/狭窄的情况下,ICG清除试验有助于发现缺血再灌注损伤导致的缺血性胆道病变(胆道畸形和狭窄),ICG血浆清除率有助于预测肝移植后缺血性胆道病变引起的移植植物损伤;另外,ICG即时清除率的测量和荧光可见性

还可以用于肝移植的肝功能评估和动脉、静脉和胆道结构的实时评估,移植前供体移植植物质量和代谢功能和肝移植后预测受体预后<sup>[56]</sup>。总之,在肝移植中,ICG在胆道成像、肝功能评估、灌注评估和评估移植后肝血管通畅性等方面均具有一定价值<sup>[13,43,57]</sup>。

## 8 ICG荧光成像技术在防治胆道损伤的应用价值

胆道损伤是较严重的手术并发症。术中对肝外胆道的误判是造成胆道损伤的主要原因<sup>[58]</sup>。胆道损伤导致胆漏、黄疸、胆道狭窄等,常需多次手术干预<sup>[59]</sup>。LC导致的胆道损伤对患者再次住院率、术后生活质量和预后均有显著不良影响,并可导致医患纠纷<sup>[26,60]</sup>。因此在胆道外科手术中寻找一种术中可清晰辨认胆道解剖结构的胆道成像方法非常必要。Dip等<sup>[61]</sup>研究显示:LC中荧光组中显示肝外胆道解剖结构效果优于白光组。ICG荧光技术可清晰显示胆囊管、胆总管等胆道解剖结构,该技术的术中胆道成像可减少胆道损伤风险<sup>[62]</sup>。系统评价提示,ICG荧光成像技术可以显著提高重要胆管解剖结构的显示率,有助于防治胆管损伤<sup>[63-64]</sup>。ICG荧光胆道成像技术具有可行性,有望成为预防胆道损伤的一种可选择途径。

## 9 ICG荧光成像技术在胆漏检测的应用价值

在肝胆外科手术中,胆漏的发生率为4.0%~13.8%<sup>[65]</sup>。Kaibori等<sup>[66]</sup>对102例病人的研究中,对照组(n=50)采用肉眼观察和研究组(n=52)使用ICG荧光胆道成像技术,研究结果显示对照组胆漏发生率为10%,ICG胆道成像研究组无发生胆漏,说明ICG胆道成像技术能较好地预防肝切除术后胆漏。有研究使用ICG荧光技术在肝切除手术中检测胆漏,也可减少术后胆漏的发生<sup>[67]</sup>。

## 10 不足及展望

在胆道外科手术中,ICG荧光成像技术有其优势的一面,但也要客观地认识其存在的局限性。ICG荧光成像技术对于>10 mm的组织结构(如胆管周围脂肪较厚、炎症水肿、肿瘤等)无法清楚地识别,因而ICG胆道成像应用也受到显著影响<sup>[15,68]</sup>。ICG静脉或胆管注射成像模式各有优缺点,如何选择最佳的给药时间、剂量选择依然有争议,未来仍需继续探索,进而充分发挥ICG荧光成像技术在胆道外科的价值。

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