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• 综 述 •

儿童供肝在肝移植胆管重建术中的研究进展

颜 科^{1,2}, 李乾国²综述, 杜成友¹审校(1. 重庆医科大学附属第一医院肝胆外科, 重庆 400016; 2. 重庆市南岸区人民医院普外科 400060)

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原发性肝癌是全世界五大恶性肿瘤之一,其发病原因多元化,在国外主要以丙型肝炎、酒精性肝病和血色病为主^[1],而在我国由于乙型肝炎病毒的蔓延、烟酒及工业污染的泛滥、饮食安全等多因素的作用下,我国成为肝癌患者最多的国家,且年轻化趋势明显^[2]。尽管随着科技的进步,放化疗及靶向治疗在一定程度上延长了患者的生存期^[3-5],晚期肝癌患者预后还是很不理想。对于早期肝癌来说,肝移植已成为公认的治疗肝癌的优先选择,肝移植患者的 5 年生存率约为 75%,但供体和胆管并发症是影响预后的主要因素。近年来儿童供肝成人移植胆管重建成为移植界的热点话题,现将儿童供肝成人移植胆管重建技术的进展作如下综述。

1 供体的选择

关于实行肝移植胆管重建术的首选类型是在移植界还没有完全达成共识。国外研究者在分析了 384 例活体供肝和 216 例尸体供肝移植术后,发现活体供肝的生存期略长于尸体供肝,相对而言并发症更多^[6]。死者器官的捐赠并不容易,需要患者本人及家属的知情同意,且受到时效性和死者本身疾病等因素的限制^[7],因此并未广泛应用;活体供肝来源相对比较广泛,主要来源于与患者有血缘关系的亲属,其次是与受体相匹配的其他捐赠者;由于肝的再生能力较强,研究已证实使用活体供肝在捐赠者身上的安全性。活体供肝尽管在肝癌移植

术中的可行性更大,但是要降低胆管并发症仍然存在着不少的技术挑战^[8]。

2 胆道并发症影响因素及处理

虽然多年来一直在不断改善肝移植术后生存率,但移植后不良反应的发生仍然是患者死亡的主要原因之一。其中一个最重要的并发症是急性排斥反应,其他主要不良事件有动静脉狭窄和血栓形成、胆管狭窄与胆管漏、丙型肝炎病毒感染疾病和肿瘤复发等^[9]。其中胆道不良事件是肝移植胆管重建术最常见的并发症,多变量分析表明,移植前血清肌酐和动脉缺血超过 30 min 是肝移植胆管重建术后的独立风险因子^[10]。胆管吻合口狭窄可能的原因有三,即血液供应受损、胆道异常和技术的缺陷。胆管狭窄的发生率在高级别医师和初级医师中差别不大,然而胆漏的发生率在初级医生的患者比那些资深外科医生更高,因此提高技术水平和增加临床经验在减少胆漏的发生率上也有着很重要的作用^[11-12]。Seven 等^[13]研究发现移植术后胆管并发症的总发生率为 36%,胆管吻合口狭窄是最常见的胆道并发症(42%),其次是胆漏(28%)。出现胆漏采用内镜逆行胰胆管造影(ERCP)引导下穿刺引流及支架置入球囊扩张是最常见的治疗方式,大多数是成功的。有研究发现吲哚菁绿(ICG)荧光造影可能在活体肝移植中的应用可减少胆

管并发症^[13]。

3 手术方式的选择

在肝移植早期,胆管空肠 Roux-en-Y 吻合术是胆管重建的标准术式,但有手术时间较长,容易发生腹腔感染和胆道功能恢复延迟等缺点。后来 Wachs 等提出胆管与胆管端端吻合重建胆管技术也逐渐被多数移植中心所接受。但哪种术式是首选,目前还没有相关定论。一些研究者发现这两种手术方式相比,胆管并发症的发生率没有明显的差异,胆管重建空肠 Roux-en-Y 吻合术不是胆管吻合口狭窄的独立危险因素,却是原发性硬化性胆管炎和再次肝移植胆管重建的首选^[14-20]。Yamamoto 等^[17]发现胆管端端吻合重建的活体肝移植的儿童是胆管重建一个可行的选择,并发症相对较少。Asonuma 等^[20]在肝移植后行胆管重建和胆囊造影,可以精确的指导切断胆管的位置和角度,不需要解剖右侧肝管,胆道并发症很少,保证了胆管的血液供应,也避免了胆管感染。一些研究者认为如果供体胆管超过 2 根,距离不超过 3 mm,可先行胆管整形,再与受体胆管行端端吻合;若胆管长度不够、胆管间距离较远(超过 3 mm)及供者与受者胆管之间呈锐角,采用胆管成型术可能会带来风险,肝胆管第 2 个开口的距离大于 3 mm,可用 Roux-en-Y 肠袢分别做 2 个肝管空肠吻合,也可采用供肝胆管分别与受体左、右肝管或胆囊管做 2 个吻合口的方式^[21]。Kim 等^[22]在端端吻合技术基础上进行了改进,自受体右肝管开口剖开至左肝管,修剪成漏斗形,将供体胆管吻合至受体胆管的上皮内膜从而形成套叠,该技术保证了胆管的血液供应,还使吻合的胆管口径相匹配,与传统技术相比,明显降低了胆管并发症。支架的基本原理是维持胆汁流尽,尽管 T 管引流的端端吻合可减少吻合口漏和胆实质切割面的损伤,但拔 T 管后胆漏可能导致潜在的致命性胆汁性腹膜炎,因此建议胆管细小(小于 2 mm)时才考虑选择性使用^[23]。

4 显微外科技术的使用

显微外科技术在肝移植中的应用越来越广泛,与传统移植术相比更具优势,手术创伤小,患者应激反应较轻,有利于患者身体的及时恢复;不需要钳夹胆管内壁从而避免损伤内膜;采用显微放大技术,可以很清楚地看到手术视野中的组织结构,使得胆管的重建更加精确,减少梗阻和吻合口漏的发生,手术空间更大,避免因腹腔太深造成打结不牢固。显微外科胆管重建在活体肝移植术的常规使用可降低吻合口胆管并发症^[24]。Kim 等^[25]使用胆管重建使用显微技术发现胆道重建的时间明显减少,保证了胆道血液的及时供应,特别是对于肝管直径小于 2 mm 的患者可减少再次移植率和提高生存率^[26]。Miyagi 等^[27]认为由于肝移植动脉较短、腹腔较深、操作不方便,形成动脉血栓的可能性比较大,使用显微外科技术行胆管重建可克服操作不便等困难,可同时降低动脉血栓的形成。虽然胆管重建成为活体肝移植的关键技术,但即使是显微外科也面临相当大的技术挑战^[28]。

5 成人供肝与儿童供肝

当前不论国内还是国外,儿童供肝例数都非常有限^[29],端端吻合胆管重建使用肝左叶移植在小儿活体肝移植的可行性仍然是有争议和具有挑战性的。国外研究发现成人与儿童供肝的疗效和并发症相差不大,使用端端胆管重建及 T 型支架比传统术式的生存期更长^[30]。Ⅰ型和Ⅱ解剖结构允许一整块肝门部胆管横断,吻合重建简单,但Ⅲ/Ⅳ型肝门部胆管的解剖,需要逐步行肝门部横切和复杂的移植胆管重建,因此后者并发症的发生率更大,反式吻合口胆道管的使用是为了减少胆管并发症^[31-33]。

德国学者提出儿童供肝移植具有以下优势:择期手术可保证肝组织的活性,降低手术风险;供体缺血时间较短,灌注损伤小,质量相对保证;近亲间血型相容性较高,发生排斥反应的概率更低;儿童肝活性较大,胆管相对比较小,成活率较高。但是也面临问题,儿童本身各系统发育不完善,手术风险相比成人更大,耐受性更差,活体供体来源很少,当前一般是使用儿童尸体作为供体来源。劈离式肝脏移植(SLT)可一定程度上缓解供体短缺的矛盾,尤其儿童供肝短缺的问题。陈新国等^[34]将供肝左肝静脉与形成好的肝静脉吻合,将左右支剪开后肝固有动脉和总动脉行端端吻合,左肝管行 Roux-en-Y 吻合术,取得了较好的疗效。儿童供肝应用于成人的关键问题是肝脏体积的大小和血管口径的匹配,最常见的并发症是血栓的形成,但儿童供肝的重量越低,并发症明显增加,生存期缩短。为减少儿童供肝中血管不匹配导致的并发症,目前一般采用背驮式肝移植,可避免管径差异造成的静脉狭窄^[35]。

综上所述,儿童供肝在成人肝移植胆管重建中的应用从当前的文献来看是可行和安全的,但是该技术仍然面临很大的挑战和存在争议,供体来源更是首先要解决的关键问题,其次是肝脏体积的大小、血管口径和血型相容。至于远期生存,仍需要大量的样本来研究证实。

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