

晚期肝门部胆管癌伴门静脉狭窄门静脉支架置入术的治疗现状

周海峰, 王海久*

青海大学附属医院普外二科, 青海 西宁

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摘要

肝门部胆管癌的发病率逐年上升, 由于起病隐匿导致疾病发现晚, 即使有手术机会, 但因手术难度大、根治率低、术后易出现并发症等因素, 5年生存率不足30%。晚期或复发的肝门胆管癌常伴门静脉狭窄或闭塞。门静脉主干或第一级分支狭窄/闭塞, 可造成肝功能损伤、腹水、食管胃底静脉曲张出血、血小板减少等并发症。这些并发症不仅会导致患者生活质量低下, 甚至会危及患者生命。对肝门胆管癌患者的影响更为重要, 可导致患者预后不良, 生存时间大幅缩短。因此, 解除门静脉狭窄是治疗此类问题的关键。本文就介入治疗晚期肝门胆管癌伴门静脉狭窄的临床疗效作一综述, 并进一步展望介入治疗在后期患者抗癌治疗、提高患者生存质量等方面的临床应用价值。

关键词

肝门部胆管癌, 门静脉狭窄, 门静脉支架

Current Status of Portal Vein Stenting in the Treatment of Advanced Hilar Cholangiocarcinoma with Portal Vein Stenosis

Haifeng Zhou, Haijiu Wang*

Department II of General Surgery, Affiliated Hospital of Qinghai University, Xining Qinghai

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*通讯作者。

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Abstract

The incidence of hilar cholangiocarcinoma is increasing year by year. Late detection of hilar cholangiocarcinoma is due to hidden onset. Even if there is an opportunity for surgery, the 5-year survival rate is less than 30% due to the difficulty of surgery, low radical treatment rate and post-operative complications. Advanced or recurrent hilar cholangiocarcinoma is often accompanied by portal vein stenosis or occlusion. The main portal vein or the first branch stenosis/occlusion, can lead to liver injury, ascites, esophageal and gastric varices bleeding, thrombocytopenia and other complications. These complications will not only lead to poor quality of life of patients, but even endanger patients' lives. The effect on hilar cholangiocarcinoma patients is more important, which can lead to poor prognosis and greatly shorten survival time. Therefore, the removal of portal vein stenosis is the key to the treatment of such problems. This article reviews the clinical efficacy of interventional therapy for advanced hilar cholangiocarcinoma with portal vein stenosis, and further looks forward to the clinical application value of interventional therapy in anti-cancer treatment and improving the quality of life of patients in the later stage.

Keywords

Hilar Cholangiocarcinoma, Portal Vein Stenosis, Portal Vein Stent

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1. 引言

肝门部胆管癌(Hilar cholangiocarcinoma, HCCA)也称 Klatskin 瘤, 是胆道系统常见的恶性肿瘤, 是一种严重的疾病, 需要通过手术切除进行治疗, 以实现长期生存[1] [2]。然而, 早期诊断往往很困难, 大多数病例确诊时已发展为晚期。晚期肝门部胆管癌往往会导致门静脉狭窄(常侵犯主门静脉(PV)): 包括周围肿瘤的肿块效应、肿瘤直接侵犯 PV 或癌症患者高凝状态下 PV 血栓形成。这些因素都会导致门静脉血流阻力增加, 肝脏血供减少, 从而导致 PV 系统压力增加, 从而导致门脉高压。可能引起各种并发症, 如食道、胃或小肠静脉曲张; 腹水的形成; 脾肿大; 血小板减少症; 肝功能不全。这些并发症不仅会导致生活质量差, 还会危及生命。从而导致后续的抗癌治疗无法进行, 使治疗难度提高, 并且使患者的总生存期受损。针对以上患者 PV 支架置入是一种可行的方法, 可以缓解 PV 狭窄患者因各种原因引起的门静脉高压症状, 如肝功能损伤、腹水、难治性食管胃底静脉曲张出血等并发症。放置门静脉支架不但打通了狭窄的门静脉, 使肝脏的主要血供恢复, 还为患者后续的抗癌治疗提供一个更好的时间窗。并且多位研究人员报告了成功使用 PVS 治疗恶性 PV 狭窄的病例, 并获得了良好的疗效[3]-[8]。PV 支架置入有助于解决与门静脉高压相关的问题, 并为后续抗癌治疗提供了一条可行的通路, 从而提高患者的总生存期(OS)。因此, 维持 PV 血流对于肝门部胆管癌患者的生存可能更为重要。

2. 肝门部胆管癌的病因

肝门胆管癌是指胆总管起始部以上, 肝总管、左右肝管及其汇合部发生的肝外胆管癌, 也称高位胆管癌或近端胆管癌, 约占肝外胆管癌的 50%~60% [9], 近年来发病率有增加趋势, 目前认为与肝胆管结

石、原发性硬化性胆管炎、先天性胆管囊性扩张症、肝吸虫感染、溃疡性结肠炎以及乙型、丙型肝炎感染等有关。病理上该病呈浸润性生长,可沿神经间隙、淋巴结及血管间隙生长,也可沿胆管壁内蔓延,与肝门区血管密切相关,手术切除困难,治疗效果不理想。

3. HCCA 分型与分期

HC 的分期首先由 Bismuth 等人描述[10]在 1970 年,基于双脑梗阻的水平,仍然是最常见的系统。虽然它是一种形态学分类,但它被广泛用作分期系统。秘等[10]将 HC 分为 4 种类型,其中 1 型涉及肝外导管,2 型涉及肺门,3A 型涉及右导管的肺门,3B 型涉及左导管的肺门,4 型涉及肺门,以及左右导管系统。尽管其有效性已被证实,但其局限性在于无法预测远处转移、淋巴结和血管受累以及随之而来的肺叶萎缩以及随后的患者生存。

4. 肝门胆管癌的诊断

肝门部胆管癌的早期症状通常是非特异性的,可能表现为血液检查异常,如肝功能异常。患者常被发现碱性磷酸酶或 γ -谷氨酰转移酶升高[11]。黄疸通常是最常见的症状,有时可能先于瘙痒[12]。此外,临床症状包括发烧、寒战、体重减轻、恶心、呕吐和不适。在某些情况下,恶性梗阻可导致上行性胆管炎、革兰氏阴性败血症和肝脓肿[13]。由于病理学证据获取困难,HC 的诊断以往多依赖于超声、CT 及 MRI,以内镜为基础的诊断技术如超声内镜(endoscopic ultrasonography, EUS)、胆管内超声(intraductal ultrasonography, IDUS)、经口胆道镜(per oral cholangioscopy, POCS)以及细胞学诊断技术和 ERCP 技术的发展有助于 HC 的进一步确诊。内镜下逆行胰胆管造影术(ERCP)和 EUS 已成为诊断和分期胃肠道病变的主要工具。ERCP 可进行透视成像、组织取样和梗阻治疗[14]。EUS 用于评估胆道狭窄、恶性肿瘤(如胆管癌)的分期,并允许对胆道疾病或肝内肿块进行组织活检[15]。EUS 在补充腹部成像模式(如磁共振成像)方面发挥着关键作用[16]。这导致了胰胆肿块的肿瘤管理和治疗方式的改进[17]。虽然 ERCP 是目前干预的主要技术,但它受到其通过透视可视化结构的能力的限制[18]。ERCP 的既往研究表明,细胞学刷洗和活检的敏感性较低,联合使用时敏感性为 59.4% [19]。然而,胆管镜检查的最新发展改善了胆道的可视化[20]。数字系统(SpyGlass 系统; Boston Scientific Corporation, Natick, MA, USA)允许更轻松、更广泛地使用[21]。SpyGlass 通过改进靶向组织活检提高了诊断准确性[22]。一项包括 10 项研究和 456 名患者的系统评价发现,胆管镜引导下活检诊断肝门部胆管癌的汇总敏感性和特异性分别为 60.1%和 98% [23]。Tyberg 等人[24]发现术前胰胆管镜检查导致 30%的胆道病变患者的手术计划发生变化。在另一项研究中,胆管镜引导下标测活检的总体成功率为 88%,无并发症[25]。

5. 肝门部胆管癌伴门静脉狭窄的原因

肝门部胆管癌引起的门静脉狭窄(Portal vein stenosis, PVS)因素包括周围肿瘤的占位效应、肿瘤直接浸润门静脉(Portal vein, PV)、术后 PV 纤维化或癌症患者高凝状态引起的 PV 血栓形成等,这些因素可导致门静脉血流阻力增加和肝脏血供减少, PV 系统压力增加,导致门静脉高压而引起各种并发症;例如由胃肠道出血、腹水、血小板减少和/或肝功能不全引起的难治性贫血,这些并发症往往患者病情恶化,从而影响患者接受后期癌症治疗[26]。

6. 肝门部胆管癌伴门静脉狭窄目前治疗方法

解除门静脉狭窄是避免或减少上述问题出现的关键所在,目前的治疗方法主要有抗凝、全身及局部溶栓、经皮门静脉再通、经颈静脉肝内门静脉分流、门静脉支架置入术等[27]。抗凝、全身及局部溶栓,可使部分血栓溶解患者症状缓解,但对门脉高压易出血患者存在较高风险,因此应用有限。外科治疗如

切开门脉取栓等虽可恢复门脉血流, 但术后并发症和病死率较高, 适应症较严格。而门静脉支架治疗可通过微创的手段开通狭窄闭塞的门静脉, 直接解除阻塞, 恢复门静脉血流, 门静脉高压不但得到改善, 临床症状也能得到缓解, 还使患者损伤最小, 受益最大。

7. 晚期肝门部胆管癌伴门静脉狭窄门静脉支架的应用

Takashi Mizuno 等人[28]报道了 10 例肝门部胆管癌经手术切除后复发的患者, 9 例接受了门静脉支架置入术, 术后患者门静脉高压的相关症状完全消失, 生活质量也得到提高, PV 支架维持了肝脏血流, 缓解了复发性肝门周围胆管癌引起的严重 PV 狭窄患者的临床症状, 并为患者后期接受可持续的抗癌治疗提供了更好的机会, 后期接受可持续抗癌患者获得了 14 个月的中位生存期, 相反, 1 例未接受门静脉支架置入术的患者因肝脏血流无法再通, 预后较差, 生存期不到 6 个月。研究表明, 肝门部胆管癌切除后复发率高, 局部复发常常涉及残留肝脏的肝流入, 并容易导致门静脉狭窄。对于复发患者, 建议全身化疗或放疗, 然而, 与 PV 狭窄相关的症状, 如由胃肠道出血、腹水、血小板减少和/或肝功能不全引起的难治性贫血, 往往会加重患者的一般状况, 因此无法进行可持续的抗癌治疗。PV 支架置入是复发性肝门部肿瘤伴 PV 狭窄患者的重要治疗方法。并且门静脉支架置入术具有创伤小、痛苦轻、恢复快、并发症少等优点。在治疗各种良恶性疾病引起的门静脉狭窄疗效好, 术后门静脉通畅度高。让门静脉狭窄患者越来越容易接受, 同时更加完善和优化了临床相关疾病的诊疗策略。

8. 总结与展望

介入支架置入术经过近 30 年的临床应用, 已经被广泛应用和接受, 门静脉支架置入术已成为肿瘤因素及非肿瘤因素所致门静脉狭窄/闭塞引起的门静脉高压相关并发症治疗的一种有效手段。当前门静脉支架已广泛应用于肿瘤性及非肿瘤性因素所致门静脉狭窄/闭塞引起的食管胃底或小肠静脉曲张、腹水、脾肿大、血小板减少和肝功能不全的治疗。明显提高了此类患者的生活质量和生存期。在以上因素所致的门静脉狭窄中, 尤其是恶性肿瘤所致的门静脉狭窄, 门静脉支架置入不但可以缓解患者门静脉高压症状, 改善生活质量和维持后续抗癌治疗, 还可以为今后原发病的治疗提供更多的治疗机会, 延长患者的生存期。但目前门静脉支架置入后支架再狭窄/闭塞的因素及解决方案仍需进一步的研究。目前对支架置入术后抗凝治疗的意见也各不统一, 需要进一步的前瞻性研究以阐明预防性抗凝的有效性。

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