

肝静脉栓塞在肝脏手术中的应用进展

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摘要

近年来随着新设备、新技术的不断出现, 肝静脉栓塞因为其较小的损伤和较高的安全性逐渐成为治疗肝胆恶性肿瘤的重要手段之一。本文通过总结已发布的文献, 介绍了肝静脉栓塞(hepatic vein embolization, HVE)在肝脏恶性肿瘤中应用的发展。

关键词

肝静脉栓塞, 肝切除术, 残肝再生

Progress of Hepatic Vein Embolization in Liver Surgery

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Abstract

In recent years, with the emergence of new devices and techniques, hepatic vein embolization has gradually become one of the most important means of treating hepatobiliary malignant tumors because of its lesser damage and higher safety. In this article, the development of hepatic vein embolization (HVE) application in hepatic malignancies is presented by summarizing the published literature.

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Keywords

Hepatic Vein Embolization, Hepatectomy, Future Liver Remnant Regeneration

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1. 术前肝静脉栓塞(HVE)代替肝切除术中的肝静脉重建

在肝癌患者中,肝切除术是常用的治疗方法。但在切除位于肝右叶上段(第7和第8节段)肿瘤时可能需要切除无肿瘤的右叶下段的肝静脉。对于肝功能正常的患者来说,无肿瘤的下节段可以像标准右肝切除术一样安全地纳入切除段,必要时还可以扩展到肝中静脉。但对于肝硬化患者而言,应尽量尝试保留无肿瘤的下段。主要原因是肝硬化患者肝脏储备功能较低,肝切除术后死亡率较高[1]。虽然许多病例可以通过相邻肝段侧支静脉流出[2],但也有一些病例需要重建肝静脉以维持足够的肝功能。而肝静脉重建使得手术时间更长,增加术中和术后出血风险。一系列的肝和血管联合切除术报告的死亡率为11%~25% [3] [4]。

2002年, Ku Y. [5]发现狗的肝静脉节段性结扎2周后,肝静脉周围有许多静脉祥形成。并将这一发现应用于肝切除术时避免行肝静脉重建的研究中,他在比特犬肝切除前两周行肝静脉栓塞。HVE手术经右颈外静脉进入,荧光控制下将球囊推入肝静脉上方。将7~10毫升半强度的造影剂注入球囊中,随后静脉打入造影剂以获得肝脏静脉的解剖学信息。将球囊内造影剂抽出后,在透视引导下将导管推进到左肝静脉,当球囊达到左肝静脉近心端时,用3~4毫升半强度的造影剂充满球囊,实现闭塞。在球囊处于最佳封堵位置时,通过输送三到四个12毫米的纤维铂金微线圈对左肝静脉近心端进行栓塞。最后,将球囊导管撤回到下腔静脉中,并进行逆行肝脏闭塞静脉造影,以确认用线圈完全闭塞左肝静脉。此研究证实HVE促进了肝静脉间侧支的形成,并能成功避免肝切除时的肝静脉重建,最大限度地减少了分段肝静脉切除的不良影响。

肝右静脉(right hepatic vein, RHV)切除术通常需要切除整个右后段。然而,广泛的肝右下静脉(inferior right hepatic vein, IRHV)的存在允许保留该段。Nakamura S.和 T. Tsuzuki [6]发现,在83份尸检材料中,20%至24%的肝脏存在广泛的IRHV。临床上,约10%的患者可通过腹部超声检查观察到IRHV [7]。1987年, Makuuchi M. [8]等人提出了保留IRHV的左三肝联合RHV切除的可能性。Baer H.U. [9]等人于1991年首次对较大肝癌患者进行了这种新的肝切除术,之后 Ozeki Y. [10]等人在1995年同样进行了此切除术。这些手术的成功表明当存在广泛的IRHV时,保留IRHV的左三肝联合RHV切除是可行的。

Nagino M. [11]报道了一例肿瘤累及肝门、左侧门静脉脐部、肝右静脉、肝中静脉和肝左静脉被完全闭塞的肝内胆管癌手术切除左三肝及RHV的患者。该患者存在IRHV,为了避免肝切除后的RHV重建,术前进行RHV栓塞。为了提高扩大肝切除术的安全性,在RHV栓塞的同时进行了左侧门静脉栓塞(portal vein embolization, PVE)。21天后按计划行左三叶和尾状叶切除伴扩大淋巴结切除。整体切除了RHV远端6 cm,成功保留了IRHV。此项研究证明人类门静脉和肝静脉同时栓塞是安全可行的。在这之前 Kaman J. [12]就使用猪研究了肝静脉结扎的效果,发现早在分段肝静脉结扎后7天,受影响的肝段就从充血中恢复了形态和功能。

2. 顺序门静脉栓塞联合肝静脉栓塞用于肝切除术前的肝脏准备

门静脉栓塞(PVE)可导致栓塞肝叶缩小和非栓塞肝叶代偿性增大,有助于改善广泛肝切除患者的预后。虽然 PVE 对术后结果有有益影响,但并非能诱导所有患者非栓塞叶充分再生[13] [14] [15]。如果未来剩余肝脏(future liver remnant, FLR)体积太小,即使在 PVE 后很长时间内仍存在术后肝功能衰竭的风险,所以不宜行肝切除。在接受 PVE 的患者中,已经测试了几种辅助治疗方法增加 FLR 容量。少数患者在 PVE 后对同侧肝动脉进行栓塞,结果并不理想,还增加了肝脓肿的风险[16] [17] [18]。尽管选择性肝内无水乙醇胆道消融可导致灌注肝叶萎缩和非灌注肝叶增生[19],但 FLR 内胆管损伤的风险很高。由于有门静脉联合肝静脉栓塞的先例,一种新的残肝再生方法逐渐被发现。

Lee S.S. [20]在一项肝移植研究中意外发现,移植肝叶门静脉闭塞同时出现肝静脉狭窄的患者对侧肝脏有增大迹象。肝静脉流出道闭塞对肝实质的影响也在使用右叶移植时不进行肝中静脉(MHV)重建的 LDLTs 中得到证实[21]。Hwang S. [22]将以上理论运用于 PVE 后残肝再生不能达到肝切除术要求的肝癌患者中。对 PVE 后 1 或 2 周 FLR 仍小于 TLV40%的患者行 RHVE,并在 HVE 2 周后行预期肝切除术。9 例接受肝切除术患者,FLR 体积占总肝体积比率从 34.8%增加到 44.2%。HVE 后 FLR 增加了基础 FLR 的 14.2%。作者观察到 RHVE 后 2~4 周内,左肝体积的增加伴随着右肝体积的减少,但总体积几乎不变 [23] [24] [25] [26]。大多数因各种肝胆疾病接受 PVE 的患者中都观察到了这种程度的叶间容积变化。

自此之后肝静脉栓塞正式被接受用于肝切除术前的肝脏准备。紧接着 Ko G.Y. [27]对门静脉联合肝静脉栓塞的血流动力学进行了分析,众所周知栓塞静脉和相邻静脉之间会形成多个静脉侧支[11],Ko G.Y.表示侧支可能抑制进一步的肝损伤。因此肝静脉末端和分支栓塞可能是诱导进一步肝再生的最佳方法。所以后来液体栓塞剂也被加入到肝静脉栓塞中。2013 年, Munene G. [28]首次报告顺序门静脉栓塞联合肝左、中静脉栓塞的病例。患者为结直肠癌肝转移需行扩大左半肝切除术以实现 R0 切除,但因患者肝脏脂肪变性且残肝不足。所以在左门静脉栓塞术后三周行左肝静脉栓塞术,左肝静脉栓塞后 1 周以类似方式进行肝中静脉栓塞,肝中静脉栓塞后四周使用相同切口行扩大左半肝切除术并顺利出院。此项研究也为后来的扩大肝静脉剥夺术(extended liver venous deprivation, eLVD)奠定了基础。

3. 同时门静脉栓塞联合肝静脉栓塞用于肝切除术前的肝脏准备

2016 年, Guiu B. [29]为了缩短等待时间,将门静脉和肝静脉栓塞术同时进行,并在用血管塞的基础上加入液体栓塞剂,同样显示出较好的增生效应。Guiu B.将此项技术正式命名为肝静脉剥夺术(liver venous deprivation, LVD)。次年 Guiu B.将肝中静脉栓塞加入肝静脉剥夺术,并将之命名为扩大肝静脉剥夺术(eLVD) [30]。他表示使用尺寸至少超过血管直径 50%的 AmplatzerII 血管塞能大大降低血管塞迁移风险。

之后关于肝静脉联合门静脉栓塞的研究层出不穷,但肝静脉栓塞的具体方法可能有些许差异。主要分为两种:1)以 LVD 为代表的经皮经肝入路,栓塞材料为 AmplatzerII 血管塞和碘油/胶水混合物。AmplatzerII 血管塞栓塞肝静脉主干、碘油/胶水混合物栓塞肝静脉末端和小分支;2)以双栓塞[31]为代表的经颈静脉入路,栓塞材料为 AmplatzerII 血管塞。AmplatzerII 血管塞栓塞肝静脉主干无需栓塞肝静脉末端和小分支。由于栓塞方式的不同两者对残肝再生的影响可能也不同,但目前没有关于两者差异的研究。

4. 肝静脉闭塞联合 ALPPS 用于肝切除术前的肝脏准备

除了 PVE 外 ALPPS 技术同样能增加残肝体积,而且 ALPPS 对残肝的增生作用高于 PVE,但发病率和死亡率较高[32]。既然门静脉栓塞能联合肝静脉栓塞促进残肝再生,有人构想 ALPPS 是否也能同肝静脉闭塞联合用于残肝再生。2021 年, Dondorf F. [33]认为在 ALPPS 手术的第一步中同时结扎肝中静脉

(MHV)和右门静脉应伴有 FLR 进一步增生。他在 20 例肝癌患者 ALPPS 手术第一阶段进行了额外的肝中静脉结扎(MHV)。MHV 结扎组(54.9%, 8.5 天)残肝再生与常规 ALPPS 组(49.9%, 10 天)相比的优势是明显的, 但不具有统计学意义($p = 0.082$)。如果只考虑结直肠癌肝转移患者, MHV 结扎组残肝增生要优于 ALPPS 组($p = 0.028$), 但 MHV 结扎组的并发症发病率较高。

2022 年, Della Corte A. [34]对 Dondorf F.的技术进行了改良。他在不进行门静脉结扎的情况下, 将腹腔镜肝脏分割(LP)与随后的 LVD 相结合, 对 5 例拟行肝大部分切除术的患者行腹腔镜肝脏分割后 5 天内行 LVD。LVD 后 28 天 4 名(80%)患者接受了计划肝切除术, 1 名患者因为腹膜转移未行手术。平均肥大率为 17%/周, 与一项有关 ALPPS 的大型研究报告的肥大率(16%/周)相当[35]。LP-LVD 术后仅记录了 1 例 3 级并发症(炎症标志物增加), 提示其具有良好的安全性。一种可能的解释是使用部分肝横断(即未到达肝门的 IVC)发病率低于全肝横断(38.1%对 88.9%) [36]。部分肝横断的另一个优点是没有手术剥离肝门, 这使得腹腔镜下肝切除术更加可行。虽然肝静脉闭塞与肝脏分割以不同形式的联合对残肝有较好的增生效益, 但现有发表的研究甚少。可能是因为与 LVD 相比其操作复杂并发症发生率高, 所以肝静脉栓塞现在更常被用于与 PVE 结合。

5. 结论

肝静脉栓塞随着时间的发展, 由开始的替代肝切除术中的肝静脉重建逐渐发展到增加残肝体积, 为没有条件行肝切除术的患者带来了手术希望。为临床医生在肝脏准备方面提供了新的治疗思路。

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