·综述·

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球囊阻断逆行静脉血管栓塞术在肝硬化并发症治疗中的应用

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摘要: 胃静脉曲张破裂出血与肝性脑病是肝硬化失代偿期常见且危及生命的并发症。球囊阻断逆行静脉血管栓塞术作为一种微创介入技术,近年来在胃静脉曲张和肝性脑病的临床管理中取得显著进展。本文系统综述球囊阻断逆行静脉血管栓塞术的技术原理、适应证(如孤立性胃静脉曲张、难治性肝性脑病)、临床疗效(急性出血止血率85%~95%、1年再出血率<15%、肝性脑病改善率60%~80%)及安全性(包括肾功能损伤和门静脉压力升高等并发症)。同时,探讨球囊阻断逆行静脉血管栓塞术与传统治疗方式(如经颈静脉肝内门体分流术、内镜治疗)的利弊,并评述近年来的最新技术改良,如金属圈辅助逆行经静脉闭塞术、血管塞辅助逆行经静脉闭塞术。未来研究方向应聚焦于患者选择的精准化(如基于血流动力学参数的分层)、栓塞材料的优化(如新型可降解栓塞剂的应用)及个体化治疗方案的制订,从而在提高疗效的同时降低并发症风险。

关键词: 气囊阻塞; 肝硬化; 食管和胃静脉曲张; 肝性脑病

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Application of balloon-occluded retrograde transvenous obliteration in treatment of liver cirrhosis complications

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Abstract: Gastric variceal rupture and bleeding and hepatic encephalopathy are common and life-threatening complications in decompensated cirrhosis. As a minimally invasive interventional technique, balloon-occluded retrograde transvenous obliteration (BRTO) has made significant progress in the clinical management of gastric varices and hepatic encephalopathy in recent years. This article systematically reviews the technical principles, indications (e.g., isolated gastric varices and refractory hepatic encephalopathy), clinical efficacy (an acute hemostasis rate of 85% — 95%, a 1-year rebleeding rate of <15%, and an improvement rate of 60%—80% for hepatic encephalopathy), and safety (including complications such as renal impairment and elevated portal vein pressure) of BRTO. Meanwhile, this article discusses the advantages and disadvantages of BRTO and conventional treatment modalities (e.g., transjugular intrahepatic portosystemic shunt and endoscopic treatment) and reviews the latest technological improvements in recent years, such as coil-assisted retrograde transvenous obliteration and plug-assisted retrograde transvenous obliteration. Future research should focus on the precision of patient selection (e.g., stratification based on hemodynamic parameters), the optimization of embolic materials (e.g., application of new biodegradable embolic agents), and the development of individualized treatment regimens, so as to improve efficacy and reduce the risk of complications.

Key words: Balloon Occlusion; Liver Cirrhosis; Esophageal and Gastric Varices; Hepatic Encephalopathy

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球囊阻断逆行静脉血管栓塞术（balloon-occluded retrograde transvenous obliteration，BRTO）是一种介入治疗方法，通过将球囊导管置入分流道的流出静脉（如胃肾分流），阻断血流后，逆行注入硬化剂至曲张静脉，从而实现其闭塞[1-11]。研究表明，BRTO治疗胃静脉曲张（gastric varices，GV）及肝性脑病（hepatic encephalopathy，HE）具有良好的临床效果[12-13]。该技术最早在亚洲（如日本、韩国）广泛应用，Olson等[14]在1984年首次发表了采用球囊闭塞硬化技术治疗GV的尝试，成功通过经股动脉入路并注入纯酒精完成球囊闭塞硬化治疗。随后，Kanagawa等[1]在20世纪90年代初进一步发展了BRTO的概念，并最终提出了BRTO这一术语。随着技术推广，欧美也逐渐应用并发展出多种改良术式，如血管塞辅助逆行经静脉闭塞术（plug-assisted retrograde transvenous obliteration，PARTO）[15-17]和金属圈辅助逆行经静脉闭塞术（coil-assisted retrograde transvenous occlusion，CARTO）[18]。

1 BRTO在GV中的临床价值

1.1 GV 在肝硬化门静脉高压患者中，GV的患病率（17%～25%）和出血风险（25%）均低于食管静脉曲张（患病率85%，出血风险64%）。然而，GV破裂出血（gastric varices bleeding，GVB）往往更为凶险，常导致较高的病死率[19]。Sarin等[19]将GV分为4类：食管胃静脉曲张（gastr-oesophageal varices，GOV）1型指GV主要位于近贲门小弯侧，与食管静脉曲张相延续；GOV 2型指GV主要位于近贲门大弯侧，伴有食管静脉曲张；孤立性胃静脉曲张（isolated gastric varices，IGV）1型为不伴有食管静脉曲张，GV位于胃底；IGV 2型不伴食管静脉曲张，GV位于胃体、胃窦或幽门。GV的治疗方式包括内镜治疗、BRTO、手术（分流术）及经颈静脉肝内门体分流术（transjugular intrahepatic portosystemic shunt，TIPS）。由于GV常伴有粗大侧支循环，内镜治疗时存在困难，需根据具体情况选择疗法。

1.2 BRTO对于GV的疗效 BRTO是治疗GVB的一种有效方法，尤其适用于以下情况：（1）伴有自发性脾肾或胃肾分流道的GOV2活动性出血：BRTO通过逆行注入硬化剂，闭塞曲张静脉及分流道，达到止血目的；（2）IGV1型出血：对于不伴食管静脉曲张的IGV1患者，BRTO可针对性地处理GV，降低再出血风险；（3）二级预防：对于既往有GVB病史的患者，BRTO能显著降低再出血发生率；（4）根除曲张静脉：通过完全闭塞曲张静脉及侧支循环，BRTO可实现GV的长期消退[20]。多项研究表明[21-24]，BRTO治疗GV效果显著，具有较高的静脉曲张根除率（90.9%～96.9%）和较低的复发率。与内镜下注射硬化疗法（endoscopic injection sclerotherapy，EIS）相比，BRTO在根除IGV、预防再出血及提高患者生存率方面优势更显著。

在32例行BRTO的患者中，有31例确认静脉曲张根除且无复发[2]。日本有学者对11例24 h内接受BRTO治疗的患者进行随访，结果显示10例（90.9%）静脉曲张完全消失，另外1例（9.1%）明显缩小，平均随访1 136 d，期间所有患者均未出现再出血或复发[25]。一项对比内镜下n-丁基-2-氰基丙烯酸酯注射和BRTO治疗活动性GVB和/或高危GV的研究显示，BRTO组的再出血率更低[8]。另有研究观察了112例IGV出血患者，其中49例患者接受BRTO治疗，63例患者接受EIS治疗。比较两组患者的治疗效果（治疗后静脉曲张出血发生率、IGV再出血发生率、生存率、死亡原因及并发症）发现，BRTO在根除IGV、预防复发及降低再出血方面均优于EIS[26]。Akahoshi等[27]及国内学者[28-29]的研究进一步确立了BRTO在GV治疗中的地位。

研究指出，BRTO具有增加门静脉血流、改善肝功能的潜在优势[30-32]。Hirota等[33]对145例患者的分析显示，48%的患者术后Child-Pugh评分得到改善。Miyamoto等[31]报道，BRTO术后1个月患者肝血流量从（441±214）mL/min增至（668±299）mL/min（P<0.000 1）、吲哚菁绿清除率由（233±123）mL/min提高至（285±148）mL/min（P<0.05），这可能与门静脉血流再分布及肝脏合成功能的恢复有关。而Saad等[34]指出，TIPS可能对肝功能造成潜在损害。一项荟萃分析[35]显示，BRTO的技术成功率（96.4%）和临床成功率（97.3%）均较高，且主要并发症率仅2.6%，证实其短期安全性优于TIPS（后者并发症率可达10%～20%[34]）。Waguri等[36]在2021年系统总结了BRTO的适应证与禁忌证，并与其他方式（药物、内镜、TIPS）比较，强调其在紧急和预防性治疗中的意义价值而被广泛使用。2023年的一篇系统性综述[37]进一步肯定了BRTO在GV中的地位。综合现有证据，BRTO对肝功能较差或存在TIPS禁忌的患者具有优势。然而，BRTO术后门静脉压力升高可能导致食管静脉曲张进展或新发[33]，其复发率高达33.3%[35]。因此，术后需密切进行内镜监测，必要时联合套扎或药物预防再出血。尽管BRTO再出血控制优于传统治疗，但对比研究显示其10年累积再出血率（18.7%）仍高于TIPS（10.6%），可能与门静脉高压持续存在有关。此外，BRTO的实施依赖于特定解剖通路，缺乏合适分流道者无法接受该治疗。

2 BRTO在HE中的临床价值

2.1 HE HE是肝硬化常见的神经系统并发症，发病机制涉及门体分流（氨等毒素直接入血）和肝细胞功能障

碍(解毒能力降低)[38]。最新研究显示,HE是终末期肝病患者死亡的独立预测因子,其临床严重程度常采用西黑文分级系统[39]作为评估标准。

2.2 BRTO在难治性HE治疗中的临床价值与机制探讨

2.2.1 BRTO的病理生理学机制与适应证 Lee等[40]指出,BRTO的核心作用机制在于,通过阻断胃-肾、脾-肾、脾-腔静脉等自发性门体分流(spontaneous portosystemic shunts,SPSS),促使原本经分流道直接进入体循环的门静脉血流重新流向肝脏,进而提升有效血液灌注量。该技术不仅有助于改善肝脏代谢功能,还能减少肠道来源的氨及其他神经毒素直接进入体循环,进而缓解HE症状。因此,BRTO尤其适用于对常规药物治疗(如乳果糖、利福昔明)效果不佳的难治性HE患者,尤其是合并显著SPSS的病例。

2.2.2 短期疗效:血氨降低与肝功能稳定性 多项研究证实,BRTO在短期内可显著降低血氨水平,且不影响肝功能。一项针对6例难治性HE患者的研究显示,BRTO术后1、3、6个月的血氨水平均显著下降,而血清天冬氨酸氨基转移酶、总胆红素、白蛋白及凝血酶原时间等肝功能指标保持稳定,提示该技术不会加重肝损伤[41]。Miyamoto等[31]的短期评估结果也与此一致。

2.2.3 中期与长期疗效:HE复发率与生存率 一项纳入39例肝硬化合并HE患者的研究评估了BRTO的中期疗效,结果显示,94.9%的患者SPSS完全闭塞,术后1年无HE生存率达91.7%,且长期随访(7年)中,无HE生存率仍维持在80.8%,总生存率为64.8%[42]。这表明BRTO不仅能有效控制HE症状,还能长期维持疗效,显著提高患者生活质量。长期随访研究进一步证实,所有患者在分流道栓塞后HE症状均得到改善,且无严重并发症报告[43-44]。

2.2.4 特殊病例与安全性 一项针对97岁高龄患者的病例报告显示,BRTO成功闭合肠系膜下静脉-髂总静脉分流后,患者的高氨血症和意识障碍迅速改善,且未出现腹痛、肝酶升高或HE复发,证实了该技术在高龄患者中应用的安全性和有效性[45]。该案例进一步支持BRTO作为合并SPSS的慢性复发性HE的重要治疗选择。

综上,BRTO在难治性HE治疗中有“分流阻断”和“血流重构”的双重治疗效应。相较于传统药物(如乳果糖、利福昔明等)治疗,BRTO技术展现出更持久的临床疗效(症状缓解率提高30%~50%),且对患者肝功能(Child-Pugh评分、MELD评分)无明显负面影响。2025年一项对TIPS术后发生显性HE的列线图预测模型指出:Child-Pugh评分是TIPS术后发生显性HE的独立影响因素[46]。然而,当前证据多基于单中心回顾性研究,样本量小,缺乏随机对照,长期随访数据不足,需进一步研究优化其应用。

3 改良的BRTO新技术

PARTO和CARTO作为BRTO的改良技术,分别采用血管塞和金属圈替代硬化剂,具有操作简练、省时,栓塞精准等优点。Kim等[47]对9例急性GVB行急诊PARTO治疗,技术及临床均成功,中期随访期间无再出血发生。一项前瞻性多中心研究纳入73例患者,手术技术成功率达100%,且未报道手术相关并发症;在中位544 d随访期间,所有患者均未出现再出血或HE[17]。此外,多项研究[15-16,48-49]结果一致支持其有效性。Lee等[18]的回顾性分析显示,CARTO的技术成功率及临床成功率(定义为无再出血)均为100%;术后CT随访显示,所有患者曲张静脉缩小并完全血栓形成。在平均(384±154) d的随访期内,无1例发生再出血。最新一项多中心研究纳入来自5个国家13个中心的311例患者(其中CARTO占比69%),其1、3、4、7、10年累积生存率分别为98%、80%、68%、52%和33%,中位生存期达99个月,再出血率分别为0.9%、3.2%、4.0%、4.5%和5.4%,总体技术成功率与临床成功率分别为96.5%和95.3%,10年主要不良事件发生率仅为4.5%[50]。

CARTO和PARTO避免了硬化剂相关风险(如肺栓塞、过敏、血栓形成、肾损伤),提升了安全性。但现有研究多属回顾性或单中心,需更多随机对照试验验证长期疗效,且弹簧圈/栓塞剂费用较高,其经济性(尤其在医疗资源有限地区)需进一步评估。

4 BRTO技术局限性及应对方案

4.1 临床价值与血流动力学影响 BRTO在治疗GVB(尤其合并SPSS的患者)及分流型HE中展现出显著的临床价值。但术后门静脉压力梯度的升高可能导致门静脉血流动力学重构,进而促进新发侧支循环形成。研究显示,15%~30%的患者术后可能出现食管静脉曲张进展、难治性腹水或HE复发[47-49]。一项针对1 016例BRTO患者的荟萃分析进一步证实,术后急性肾损伤(发生率为3%~8%)、硬化剂相关溶血性贫血及门静脉/脾静脉血栓形成(发生率为5%~12%)是值得关注的不良事件。尽管如此,BRTO的3年生存率仍可达75%~87.4%,凸显其在特定人群中的生存获益[34]。

4.2 技术改良与优化策略 PARTO和CARTO降低了硬化剂相关并发症风险,提高了栓塞操作效率。此外,联合治疗策略(如BRTO+TIPS)在部分门静脉高压合并多处分流的患者中展现出协同作用:既能有效控制曲张静脉出血,又能通过TIPS降低门静脉压力,从而减少腹水及EV进展的风险。

4.3 未来研究方向 (1)精准患者选择:建立基于门静脉血流动力学、分流道解剖特征及肝功能储备的决策模型;探索血氨、炎症因子等生物标志物在预测HE复发或腹水加重中的价值。(2)长期疗效与安全性:目前多数研究的随访时间不超过5年,亟需开展多中心前瞻性队列研究(如随机对照BRTO与TIPS),评估远期再出血率、肝病进展及生存差异;并需明确门静脉高压症的长期管理策略[51],例如是否需要序贯TIPS或内镜干预。(3)技术创新:开发可降解栓塞材料以减少远期血栓风险;结合人工智能(AI-based影像分析),优化分流道定位及栓塞范围的规划。

5 小结

综上,BRTO及其改良技术为肝硬化合并GVB或分流性HE患者提供了微创且有效的治疗选择,但其对门静脉系统的血流动力学影响仍需谨慎管理。未来需通过高级别证据及技术创新进一步优化治疗策略,以实现个体化的精准治疗。

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