

TIPS术后支架功能障碍的研究现状

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■背景资料

经颈静脉肝内门体分流术(TIPS)目前已经成为治疗门脉高压并发症的有效方法,特别是门静脉高压导致的急性食管胃底静脉曲张破裂出血的患者,可以起到立竿见影的止血效果,而维持手术疗效的关键是保持支架通畅。随着手术的日渐成熟和覆膜支架的应用,支架内血栓导致的TIPS功能障碍日益突出,因此术后的抗凝治疗尤为重要。

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Transjugular intrahepatic portosystemic shunt dysfunction

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Abstract

Transjugular intrahepatic portosystemic shunt (TIPS) is an effective method for the management of complications of portal hypertension, and it should be considered the first-line treatment for acute hemorrhage due to ruptured esophageal varices caused by portal hypertension. Keeping the stent unobstructed is key to the success of TIPS. Stent thrombosis is one of the main reasons for TIPS dysfunction. There has been no mention of TIPS postoperative anticoagulation in both domestic and foreign anticoagulation guidelines, because the consensus has not been reached yet. This paper reviews recent advances in research of TIPS dysfunction.

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Key Words: Transjugular intrahepatic portosystemic

shunt; Shunt dysfunction; Anticoagulation

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摘要

经颈静脉肝内门体分流术(transjugular intrahepatic portosystemic shunt, TIPS)目前已经成为治疗门脉高压并发症的有效方法,特别是门静脉高压导致的急性食管胃底静脉曲张破裂出血的患者, TIPS应作为一线治疗方案。而维持手术疗效的关键是保持支架通畅。支架内血栓形成是TIPS功能障碍主要原因之一。目前国内外相关的抗凝指南中均未提到TIPS术后抗凝治疗,也没有达成共识。本文就TIPS支架功能障碍作一综述。

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关键词: 经颈静脉肝内门体分流术; 支架功能障碍; 抗凝治疗

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0 引言

我国是肝病大国,各种肝病最终可能发展为肝硬化甚至肝癌。终末期肝病给患者家庭和社会造成很大的经济负担和社会负担。肝硬化的年发生率17/10万,主要累及20-50岁男性,城市男性50-60岁肝硬化患者的病死率高达112/10万,肝硬化造成门脉高压引起的食管胃底静脉曲张破裂出血是主要死因之一。经颈静脉肝内门体分流术(transjugular intrahepatic portosystemic shunt, TIPS),目前已经成为治疗门脉高压并发症的有效方法^[1-9],特别是门静脉高压导致的急性食管胃底静脉曲张破裂出血的患者优于内镜治疗^[10,11], TIPS应作为一线治疗方案^[12]。而维持

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手术疗效的关键是保持支架通畅, TIPS术中, 在穿刺过程中对血管造成创伤, 启动凝血机制, 植入的支架为异物等, 血栓形成风险明显增加。支架内血栓形成是TIPS功能障碍主要原因之一, 抗凝治疗是预防和治疗支架内血栓形成的主要方法, 但目前国内外相关的抗凝治疗指南中, 没有明确的提出TIPS术后抗凝方案, 也没有查找到的研究报道。但是随着TIPS术的成熟及推广, 迫切需要对TIPS围手术期及术后患者的抗凝治疗进行研究, 为TIPS患者的抗凝治疗提供更客观的依据。

支架功能障碍是由于TIPS支架或者分流道的闭塞和/或狭窄引起的门静脉系统减压失败导致TIPS术前的症状体征再出现。判断标准以支架狭窄度50%^[13-15]最为常用, 此外还有肝静脉压力梯度上升至 $>12\text{ mmHg}$ ^[15-17]、TIPS术后门脉高压并发症的复发^[18-21]等, 如: 静脉曲张破裂出血、腹水或胸腔积液等。临床上, 部分支架再狭窄的患者, 心理负担明显加重, 影响病情发展, 对治疗失去耐心和信心, 患者的生活质量明显受影响。

1 TIPS术不同时期影响因素

1.1 早期狭窄闭塞的因素 早期支架障碍一般是手术过程中支架释放时未完全支撑肝实质部分分流道、支架释放后扭曲成角^[22,23], 可能胆汁渗漏至支架内^[24,25], 血液处于高凝状态, 使分流道内急性血栓形成^[23,26]。手术过程造成血管组织损伤激活外源性凝血途径, 植入支架激活了内源性凝血机制, 造成急性血栓形成。

1.2 中远期狭窄闭塞的因素 支架内假性内膜过度增生^[2,23,27-30], 分流道损伤后纤维性愈合, 支架内慢性血栓形成等。

2 不同术式对支架内血流的影响

TIPS术+断流(胃冠状静脉栓塞术), 理论上, 支架内血流增加, 血栓形成几率降低; 单纯TIPS术, 理论上血栓形成几率高于断流+分流, 但研究结果显示两组不同术式的支架通畅率无统计学差异^[13]。

3 TIPS术支架狭窄的影响因素

3.1 术前因素 患者的基本情况, 包括肝功能情况、凝血功能情况、是否脾切除、门静脉血流的特殊性、肝静脉门静脉是否形成血栓、是否合并其他疾病等。

3.2 术中因素 手术过程, 涉及到血管穿刺成功率、支架的选择、支架的位置、放置的角度、门静脉左右支的选择、术中肝素的应用等。其中穿刺针在肝内的穿刺对肝脏是一种机械性损伤^[31], 血管穿刺成功率越低, 对组织血管的损伤就越高, 外源性凝血途径就越强烈, 血栓形成几率就会越高。TIPS采用覆膜支架可较裸支架明显减少术后分流道狭窄^[14,18,26,32-35], Clark等^[26]在膜支架与裸支架通畅率的研究中, 指出膜支架可以降低支架功能障碍的发生率但对患者的生存率没有影响, 但研究中没有提及术后患者是否服用抗凝药物, 而抗凝药物的应用在TIPS术后占非常重要的地位, 特别是在围手术期。选择性门静脉左支作为门腔静脉分流道, 可以显著降低肝性脑病发生率, 对保护肝功能、提高分流道远期开通率具有重要的临床意义^[36]。

3.3 术后因素 围手术期及术后抗凝治疗。而目前报道的相关文献中, 都没有统一的抗凝方案。Fanelli等^[4]在门脉海绵样变性导致的门脉高压行TIPS的研究中指出需抗凝保证支架通畅, 并参考肝硬化后TIPS术的抗凝方案, 但文章中没有具体介绍抗凝方案。Eldorrry等^[37]在布加氏综合征行TIPS的研究中提到术后的抗凝治疗, 低分子肝素24 h或普通肝素6 h后口服华法林, 使国际标准化比率(international normalized ratio, INR)值在2-3之间, 但没有说明不同患者凝血功能不同时肝素和华法林的具体用量及检测指标。国内的研究报道^[38], 只涉及到患者的肝功能分级, 没有具体到凝血功能的情况以及患者的裸支架或膜支架不同情况时的抗凝治疗。TIPS术后支架内血栓形成溶栓治疗的个案报道, 没有具体介绍TIPS术后的抗凝方案^[39]。Siewert等^[40]的个案报道, 酒精性肝硬化患者TIPS术后抗凝治疗, 随访中支架内血栓形成, 使用氯吡格雷联合低分子肝素加强抗凝治疗, 随访至一年支架保持通畅, 但该个案报道中没提及术后是否先使用低分子肝素治疗。

4 TIPS抗凝的现状

2010年AASLD实践指南中关于TIPS治疗门脉高压症, 未提出TIPS术后常规使用抗凝剂的建议^[41]。2008年美国胸科医师协会(ACCP)的抗凝治疗指南中也没有对TIPS术后的抗凝给予相应建议^[42]。英国血液学标准委员会血栓与止血分会的第三版《口服抗凝剂指南》^[43]未就TIPS术后的抗凝问题进行说明。英国血液学标准委员

■应用要点

本文从TIPS术过程及支架情况、患者自身情况和术后干预等方面阐述影响支架功能障碍的因素以及术后抗凝治疗面临的问题, 对临床研究TIPS术后支架功能障碍有重要的指导作用。

■创新盘点

本文从TIPS术的提出、临床应用到目前日趋成熟,引用大量文献,特别是近年的研究结果以阐述引起支架功能障碍的因素和近年TIPS术后抗凝治疗的现状,提供了大量有价值的信息。

会《肝素使用及监控指南》^[24]中对腹腔内静脉血栓形成的病人应考虑使用肝素治疗。如果用普通肝素,可以用小剂量,也可以用足以延长活化部分凝血激酶时间(activated partial thromboplastin time, APTT)两倍于正常对照的治疗,如果用低分子肝素,可以给常规预防剂量或治疗剂量^[24],但没指出TIPS术后围手术期及随访中支架内血栓形成时肝素的使用情况。

5 现有方案来源

5.1 借鉴肺血栓栓塞 相同点: 都是静脉血栓。不同点: 肺栓塞时其患者凝血功能、血小板(platelet, PLT)、白蛋白大多是正常的,目的是以治疗为主,抗凝药物主要是肝素加华法林,时间为3 mo^[44,45],伴有癌症、抗心磷脂抗体、凝血酶缺乏或复发的易栓症患者,抗凝治疗至少6 mo,部分患者需要长期抗凝^[45],检测INR使其在2-3之间^[46]。而行TIPS术的患者其凝血功能异常,PLT、白蛋白大多是降低,目的是以预防为主。

5.2 借鉴经皮冠状动脉介入治疗术后抗凝 相同点: 都是血管内支架,都是预防支架狭窄闭塞。不同点: 冠脉支架内形成的血栓为动脉血栓,其患者凝血功能、PLT、白蛋白一般正常,支架位置在动脉血管内,抗凝药物一般是肝素^[23]加双抗,终身服药^[27,47]。TIPS术支架内形成的是静脉血栓,患者的凝血功能异常,PLT、白蛋白一般都低于正常值,支架位于静脉血管及肝实质内。

TIPS术后现有的方案: 低分子肝素加硫酸氢氯吡格雷; 低分子肝素加阿司匹林; 低分子肝素加华法林等,而抗凝药物的选择及维持时间,目前没有达成共识。

6 肝硬化患者TIPS术抗凝治疗的特殊性

肝硬化患者凝血功能紊乱; 肝功能减退,白蛋白降低,药物与白蛋白结合率降低,药物的代谢受到影响; 同期使用药物的影响(如: 质子泵抑制剂可以延长凝血酶原时间^[48],抑酸药可增加抗凝药自尿中排泄,使血药浓度下降); 支架内为静脉血栓^[49],但门静脉血流具有自己的特殊性(血液的成分、血流速度等^[50]); 支架内压力及血流方向等,均可能影响抗凝药物的疗效。

7 结论

TIPS术后抗凝治疗借鉴于肺血栓溶栓和PCI术后抗凝治疗,上述患者的肝功、凝血功能一般正常,而肝硬化TIPS术患者的肝功、凝血功能紊乱、术前门静脉血栓情况以及是否合并高风险

血栓形成疾病等均对抗凝药物的选着、剂量、维持时间都有明显的影响,如: PLT、凝血酶原时间(prothrombin time, PT)、INR、APTT哪个或哪几个组合才是抗凝疗效的最佳检测指标; 不同术式(单纯分流、分流+断流术)的各自的抗凝方案是否相同; 裸、覆膜支架的抗凝方案是否有区别等都需相应深入研究。希望多中心合作研究,对于已经行TIPS术的患者需要加强随访,从个体治疗中摸索总结经验,为TIPS围手术期及术后规范化抗凝治疗提供依据。

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同行评价

本文综述了TIPS术后支架功能障碍的研究现状, 对临床有一定指导意义。

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