

# 球囊阻断逆行经静脉闭塞对比经颈静脉肝内门体分流治疗门脉高压胃底静脉曲张出血的 Meta 分析

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**【摘要】** 目的 采用 Meta 分析方法对比球囊阻断逆行经静脉闭塞术(BRTO)与经颈静脉肝内门体分流术(TIPS)治疗门脉高压胃底静脉曲张出血的可行性和安全性。方法 计算机检索 PubMed、EMBase 及 Cochrane 数据库,检索时限自建库至 2015 年 4 月 26 日,全面收集 BRTO 术和 TIPS 术治疗门脉高压胃底静脉曲张出血的随机对照研究和队列研究。采用 Cochrane 协作网 RevMan 5.3 软件对数据作统计学分析。结果 共纳入 5 个临床对照研究。Meta 分析显示,BRTO 术对比 TIPS 术在技术成功率( $OR=0.19$ ,  $95\%CI:0.03\sim 1.08$ ,  $P=0.06$ )、止血率( $OR=3.41$ ,  $95\%CI:0.33\sim 35.40$ ,  $P=0.30$ )和手术相关并发症发生率( $OR=1.98$ ,  $95\%CI:0.44\sim 8.84$ ,  $P=0.37$ )方面差异无统计学意义,但有更低的术后再出血率( $OR=0.27$ ,  $95\%CI:0.09\sim 0.81$ ,  $P=0.02$ )和术后肝性脑病发生率( $OR=0.05$ ,  $95\%CI:0.02\sim 0.13$ ,  $P<0.000\ 01$ )。结论 BRTO 术治疗门脉高压胃底静脉曲张出血具有较高可行性和安全性,只要合理选择病例,可能成为替代 TIPS 术治疗选择之一。

**【关键词】** 经颈静脉肝内门体分流术;球囊阻断逆行经静脉闭塞术;门脉高压症;胃底静脉曲张;上消化道出血;Meta 分析

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**Balloon-occluded retrograde transvenous obliteration versus TIPS for treatment of gastric fundus varices due to portal hypertension: a meta-analysis** PENG Lun-hua, WANG Yun-bing, GUO Can. Section I, Department of Surgery, Wanzhou Hospital of Integrated Traditional Chinese and Western Medicine, Wanzhou District, Chongqing 404100, China

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**【Abstract】 Objective** To compare the feasibility and safety of balloon-occluded retrograde transvenous obliteration (BRTO) with those of transjugular intrahepatic portosystemic shunt (TIPS) in treating bleeding from gastric fundus varices due to portal hypertension by using meta-analysis method. **Methods** The databases of PubMed, EMBase and Cochrane were included in the scope of search, and the retrieval time was from the establishment of the databases to April 26, 2015. The randomized controlled trials and cohort studies concerning BRTO versus TIPS in treating bleeding of gastric fundus varices were totally collected. The Cochrane network RevMan 5.3 software was used for statistic analysis. **Results** A total of five clinical controlled studies were enrolled in this study. Meta-analysis showed that no statistically significant difference in the technical success rate existed between the two groups ( $OR=0.19$ ,  $95\%CI:0.03\sim 1.08$ ,  $P=0.06$ ), as well as in the hemostasis rate ( $OR=3.41$ ,  $95\%CI:0.33\sim 35.40$ ,  $P=0.30$ ) and in the incidence rate of postoperative procedure-related complications ( $OR=1.98$ ,  $95\%CI:0.44\sim 8.84$ ,  $P=0.37$ ). However, BRTO carried lower incidences of post-operative re-bleeding ( $OR=0.27$ ,  $95\%CI:0.09\sim 0.81$ ,  $P=0.02$ ) and post-operative encephalopathy ( $OR=0.05$ ,  $95\%CI:0.02\sim 0.13$ ,  $P<0.000\ 01$ ) than TIPS. **Conclusion** For the treatment of gastric fundus varices bleeding caused by portal hypertension, BRTO is quite feasible and safe, it may become

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one of the alternative treatment options for TIPS as long as the patients are reasonably selected. (J Intervent Radiol, 2016, 25: 843-848)

**【Key words】** transjugular intrahepatic portosystemic shunt; balloon-occluded retrograde transvenous obliteration; portal hypertension; gastric fundus varices; upper gastrointestinal hemorrhage; meta-analysis

门脉高压胃底静脉曲张出血较少见于食管静脉曲张出血,但病情更凶险,预后更差<sup>[1]</sup>,治疗仍是难题<sup>[2-4]</sup>。经颈静脉肝内门体分流术(TIPS)常用于患者一般情况差、药物降压与止血、三腔二囊管压迫等措施无法处理的情况<sup>[5-6]</sup>。球囊阻断逆行经静脉闭塞术(balloon-occluded retrograde transvenous obliteration, BRTO)通过体表穿刺静脉内置管,经下腔静脉、左肾静脉、脾-肾分流通道或胃-肾分流通道等途径进入曲张静脉流出道远端,扩张球囊以堵塞流出道,随后对胃底曲张静脉作造影和栓塞,最终达到止血目的<sup>[7-9]</sup>。BRTO 术治疗后门静脉向肝血流并不减少,肝功能不受影响,故也可用于肝功能较差、不能耐受 TIPS 术患者<sup>[10]</sup>。然而 BRTO 术后门脉高压仍可能加重,引发相关并发症如食管静脉曲张出血及门脉高压性腹水<sup>[11]</sup>,因此其应用及适应证仍存在一定争议。BRTO 术治疗门脉高压症所致急性胃底静脉曲张出血前景仍需进一步评估<sup>[12]</sup>。

BRTO 术与 TIPS 术几乎同时诞生,只是不同国家学者认识上不一致使其在不同地方的应用各异。随着近年 BRTO 术开展与研究,文献报道中可观的疗效使其在美国逐渐流行。两种术式治疗机制虽不同,但同属介入微创术,具有良好的可比性<sup>[13-16]</sup>。Park 等<sup>[17]</sup>2015 年在一项 Meta 分析中纳入 24 篇 BRTO 相关研究文献,但均为非对照性研究文献,不能对 BRTO 术和 TIPS 术疗效作比较。目前 BRTO 术对比 TIPS 术治疗门脉高压胃底静脉曲张出血的研究尚少,多为单中心、小样本研究,疗效上缺乏一致定论;尚无疗效对比的系统评价或 Meta 分析。本研究广泛收集 BRTO 术对比 TIPS 术治疗门脉高压胃底静脉曲张出血的临床对照研究文献,对比手术前后情况,评估 BRTO 术可行性与安全性。

## 1 材料与方法

### 1.1 检索策略

计算机检索 PubMed、EMBase 及 Cochrane 数据库,检索时限自建库至 2015 年 4 月 26 日,全面收集 BRTO 术和 TIPS 术随机对照研究和队列研究。检索词包括“transjugular intrahepatic portosystemic shunt”“TIPS”“balloon occluded retrograde transvenous

obliteration”“BRTO”“B-RTO”“BORTO”和“transjugular retrograde obliteration”。

### 1.2 文献纳入与排除标准

纳入标准:①门脉高压胃底静脉曲张患者,有出血风险或是活动性出血;②干预措施如 BRTO(观察组)和 TIPS(对照组)术前基准一致并同期进行;③文献类型为随机对照研究和队列研究,文献中一般资料齐全,数据完整;④疗效判定主要指标包括技术成功率、止血率、术后再出血率、术后肝性脑病发生率、手术相关并发症发生率,次要指标包括术后发热、肝功能 Child 分级加重、5 年生存率、腹水加重、新腹水形成、胃静脉曲张消退情况。排除标准:①病例研究中无对照者,或非 BRTO 与 TIPS 对照者;②综述或系统综述文献;③同一作者重复发表(若信息能相互补充则将其补充到信息更全的一篇文章);④试验尚未完成或仅有初步结果,缺失重要研究数据。

### 1.3 文献筛选、资料提取与方法学质量评价

2 名评价员独立筛查文献、提取资料,最后交叉核对,以确保提取文献数据真实可靠、客观完整;意见不同时,通过讨论或咨询专家解决;数据不全及数据形式不同时,则与作者联系予以补充,无法获得的资料不纳入本研究。采用 Cochrane 风险偏倚评估工具<sup>[18]</sup>评价随机对照研究质量,非随机对照试验方法学评价指标(MINORS)评分法<sup>[19]</sup>评估队列研究质量。

### 1.4 统计学方法

采用 Cochrane 协作网 RevMan 5.3 软件进行统计学分析。先用  $\chi^2$  检验和  $I^2$  检验作同类研究异质性评价,用随机效应模型合并效应量,分别计算观察组和对照组技术成功率、止血率、再出血率、肝性脑病发生率、手术相关并发症发生率的 OR 值及其 95%CI。若临床试验提供数据不足,只作描述性分析,同时根据漏斗图判断发表偏倚。

## 2 结果

### 2.1 文献检索结果及纳入文献特征

根据检索策略进行数据检索,检索过程见检索流程图(图 1)。最终纳入 5 篇临床对照研究文献,其

中前瞻性随机对照研究 1 篇<sup>[20]</sup>, 队列研究 4 篇<sup>[21-24]</sup>。采用 Cochrane 质量评价方法评价前瞻性随机对照研究文献, 除了盲法与分配隐藏交代不清楚外, 其它

特点均比较满意, 考虑原始研究质量较高; MINORS 评分对队列研究作质量评价, 得分 18~20 分提示总体质量较好。纳入文献基本特征见表 1。

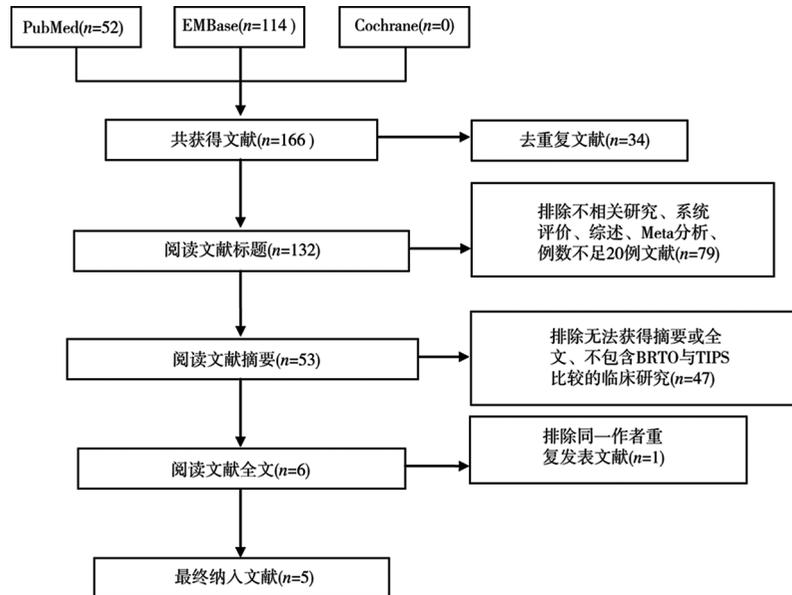


图 1 文献检索流程图

表 1 纳入文献的基本特征

纳入文献	类型	患者/例			随访时间	患者特点	结局指标
		总数	BRTO	TIPS			
Choi 等(2003 年) <sup>[20]</sup>	随机对照	15	8	7	6~21 个月(平均 14.4 个月)	活动性胃静脉曲张出血	直接止血、再出血、术后肝性脑病
Lee 等(2014 年) <sup>[21]</sup>	队列	135	86	49	平均 735 d	胃静脉曲张出血	技术成功率、再出血率、再出血原因与位置、生存率、肝性脑病与腹水
Lee 等(2012 年) <sup>[22]</sup>	队列	100	68	32	—	胃静脉曲张出血	技术成功率、再出血、肝性脑病、生存率、肝功能异常加重
Sabri 等(2014 年) <sup>[23]</sup>	队列	50	23	27	TIPS 组 1~52 个月(平均 19.5 个月), BRTO 组 1~49 个月(平均 18.2 个月)	孤立性胃出血	技术成功率、主要并发症、肝性脑病、再出血发生率
Sauk 等(2014 年) <sup>[24]</sup>	队列	52	25	27	—	孤立性胃出血	并发症发生率、再出血、新的肝性脑病、新产生腹水、再次干预、胃镜查胃静脉曲张消退

注: “—”表示原文中未见报道, 无法获得信息

## 2.2 两术式对照研究结果

2 篇临床对照研究<sup>[22-23]</sup>报道 BRTO 术(91 例)对比 TIPS 术(60 例)技术成功率, 经 Meta 分析提示各试验间无异质性( $P=0.86, I^2=0\%$ ), 随机效应模型分析显示 BRTO 术技术成功率为 87.91%, TIPS 术为 98.33%, 前者虽低于后者, 但差异无统计学意义( $OR=0.19, 95\%CI: 0.03\sim 1.08, P=0.06$ )(图 2)。

2 篇临床对照研究<sup>[20, 23]</sup>报道 BRTO 术(31 例)对比 TIPS 术(34 例)止血率, 经 Meta 分析提示各试验间无异质性( $P=0.80, I^2=0\%$ ), 随机效应模型分析显示 BRTO 术止血率为 100%, TIPS 术为 94.12%, 前者高于后者, 差异无统计学意义( $OR=3.41, 95\%CI:$

$0.33\sim 35.40, P=0.30$ )(图 3)。

4 篇临床对照研究<sup>[21-24]</sup>报道 BRTO 术(202 例)对比 TIPS(136 例)术后再出血率, 经 Meta 分析提示各试验间存在较小异质性( $P=0.11, I^2=50\%$ ), 随机效应模型分析显示 BRTO 术术后再出血率为 7.43%, TIPS 术为 22.79%, 前者低于后者, 差异有统计学意义( $OR=0.27, 95\%CI: 0.09\sim 0.81, P=0.02$ )(图 4)。

5 篇临床对照研究<sup>[20-24]</sup>报道 BRTO 术(210 例)对比 TIPS 术(141 例)术后肝性脑病发生率, 经 Meta 分析提示各试验间无异质性( $P=0.75, I^2=0\%$ ), 随机效应模型分析显示 BRTO 术术后肝性脑病发生率为 1.43%, TIPS 术为 29.79%, 前者低于后者, 差异

有统计学意义 ( $OR=0.05, 95\% CI: 0.02\sim 0.13, P<0.000 01$ ) (图 5)。

2 篇临床对照研究<sup>[23-24]</sup>报道 BRTO 术 (48 例) 对比 TIPS 术 (55 例) 相关并发症发生率比较, 经 Meta 分析提示各试验间无异质性 ( $P=0.79, I^2=0\%$ ),

随机效应模型分析显示 BRTO 术相关并发症发生率为 10.42%, TIPS 术为 5.45%, 前者高于后者, 差异无统计学意义 ( $OR=1.98, 95\% CI: 0.44\sim 8.84, P=0.37$ ) (图 6)。

对技术成功率、止血率、术后再出血率、术后肝

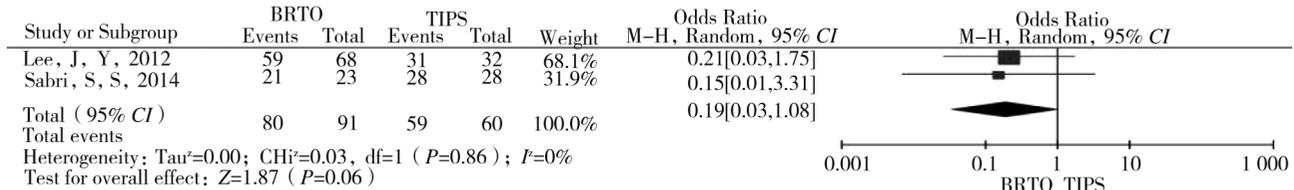


图 2 两术式技术成功率比较

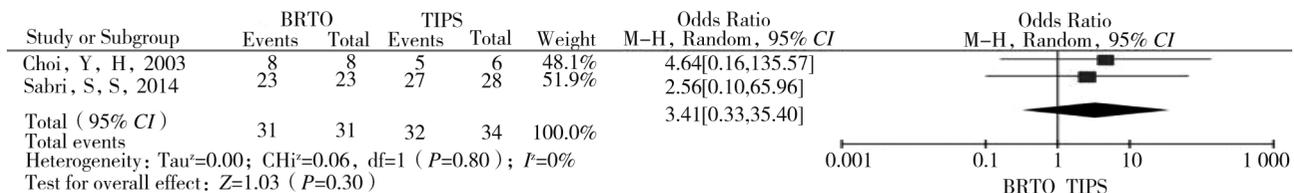


图 3 两术式止血率比较

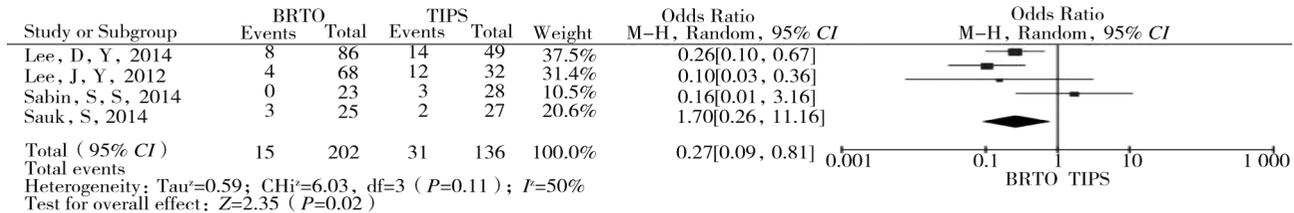


图 4 两术式术后再出血率比较

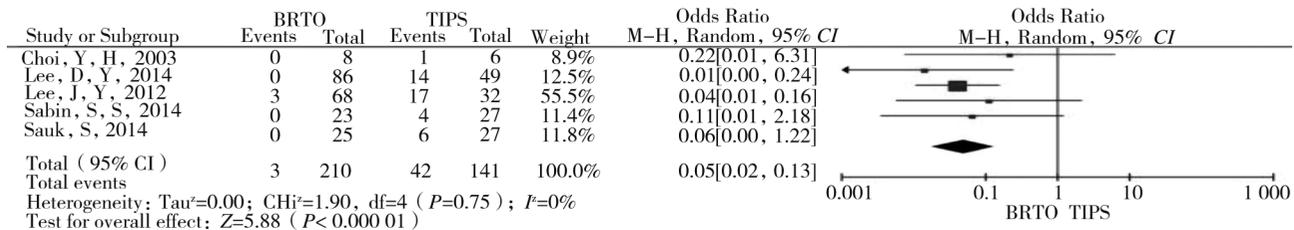


图 5 两术式术后肝性脑病发生率比较

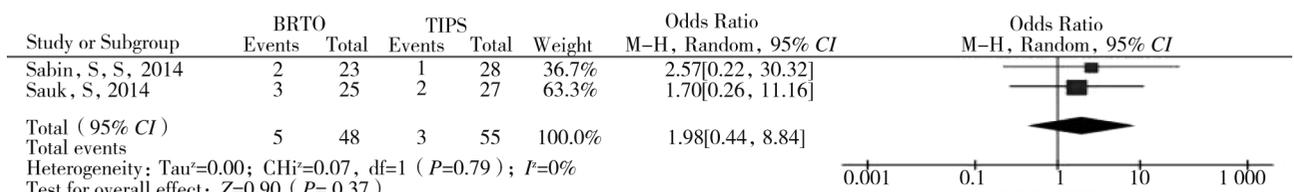


图 6 两术式手术相关并发症发生率比较

性脑病发生率和手术相关并发症发生率指标作敏感性分析, 依次单独剔除 1 篇其它文献后, 各临床试验合并效应量变化不大。改用固定效应模型对数据进行分析, 均未见 Meta 分析结果逆转。

由于纳入研究的文献总数少于 10 篇, 未作漏斗图检验发表偏倚。

### 3 讨论

TIPS 术旨在降低门脉高压、预防和治疗消化道出血<sup>[25]</sup>。BRTO 术近年受到美国学者更多关注与认可, 相关研究增多<sup>[26-30]</sup>。现有研究报道多提示 BRTO 术与 TIPS 术治疗效果相当或更佳<sup>[31]</sup>, 本研究结果也显示 ERTO 术治疗门脉高压性胃底静脉曲张出血的

安全性与可行性。

本研究比较了 BRTO 术与 TIPS 术技术成功率, 合并效应量分析提示 BRTO 术技术操作要比 TIPS 更为困难, 但差异无统计学意义。这种技术层面的难度可予克服, BRTO 术用于治疗 and 预防门脉高压胃底静脉曲张出血是可行的<sup>[32-37]</sup>。

本研究结果提示 BRTO 术可达到与 TIPS 同样的止血效果, 且能更有效地控制再出血, 降低肝性脑病发生, 同时不增加手术相关并发症发生。

本研究发现 BRTO 术后发热发生率较高, 与既往报道相符<sup>[20]</sup>。有报道显示 BRTO 术后腹水加重较多见<sup>[21]</sup>, 也有研究认为两术式间无差异<sup>[22]</sup>。另外, 有研究显示 BRTO 术后肝功能 Child 分级加重较少见, 5 年生存率较高<sup>[22]</sup>, 胃静脉曲张消退也较多见, 两术式术后新腹水产生对比则无差异<sup>[24]</sup>。这些次要指标总体上均提示 BRTO 术相比 TIPS 术呈一定优势。但以上结论仅限于单个研究结果, 且缺乏足够样本量支撑, 还需要进一步研究加以验证。

随着对 BRTO 术研究增多, 一些研究相继报道传统 BRTO 术改良术式, 结果提示可取得比传统 BRTO 术和 TIPS 术更好的疗效<sup>[38-39]</sup>, 可见 BRTO 术可能成为治疗门脉高压胃底静脉曲张出血的另一研究领域。

总之, BRTO 术治疗门脉高压胃底静脉曲张出血具有较高可行性和安全性, 只要合理选择病例, 可能成为替代 TIPS 术治疗选择之一。不过, 须认识到 BRTO 术与 TIPS 术治疗门脉高压胃底静脉曲张机制不同, 各自适应证也有些不同<sup>[40]</sup>; BRTO 术治疗尚面临诸多问题, 需更多研究不断完善<sup>[41]</sup>。

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