

食管静脉曲张出血套扎术后再出血的预防及治疗

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Progress in prevention and treatment of rebleeding after endoscopic band ligation for esophageal variceal bleeding

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Abstract

Hemorrhage from esophageal varices is a serious and common complication of decompensated cirrhosis and carries a significant rate of morbidity and mortality. Endoscopic variceal ligation (EVL) is an effective treatment for esophageal varices; however, there is a very high rate of rebleeding. Prevention and treatment of rebleeding after EVL are important for improving survival in patients with liver cirrhosis. Currently, many measures, including endoscopy, surgery, medication, and a combination of them, have been developed to prevent the occurrence of rebleeding after EVL. Many clinical trials have been done to evaluate the effectiveness of various treatments, alone or in combination, for rebleeding.

Key Words: Band ligation; Rebleeding; Esophageal varices

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摘要

食管静脉曲张出血是肝硬化失代偿期最常见也是最严重的并发症, 发病率和病死率较高. 套扎术能有效治疗食管静脉曲张, 但术后的再出血率很高. 因此, 预防套扎术后的再出血, 是提高肝硬化患者生存率的重要措施. 随着人们对套扎术后患者再出血的预防及治疗研究的不断进展, 有助于改善肝硬化这一严重并发症的结局. 目前已经开展了许多预防再出血的治疗方法, 包括内镜或手术治疗、药物治疗, 以及联合治疗方法. 关于单一方法治疗或联合治疗的效果, 已有多项试验进行了研究, 本文将对以上研究成果进行综述, 以指导临床选择适宜的预防和治疗策略.

关键词: 套扎术; 再出血; 食管静脉曲张

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0 引言

门脉高压症是导致肝硬化严重并发症的主要原因, 由此导致的食管静脉曲张出血是肝硬化失代偿期最常见也是最严重并发症, 有较高的发病率和病死率. 随着临床治疗水平的提高, 其导致的死亡率已由1981年的42%降至近期的14%-20%. 在早期死亡率中, 再出血所占比例^[1]约为50%. 因此预防套扎术后的再出血, 是提高肝硬化患者生存率的重要措施. 本文对近期关于食管静脉曲张出血套扎术后再出血的预防和治疗进展进行综述, 以指导临床选择适宜的预防和治疗策略, 提高生存率, 改善肝硬化患者的预后.

1 再出血的诊断及套扎术

依据Baveno IV标准, 早期出血时间定义为6 wk. 食管静脉曲张出血占到肝硬化患者出血的70%, 因此内镜检查是诊断食管静脉曲张出血的金标准. 食管静脉曲张出血的患者一般在内镜下可见渗血或喷射状出血, 套扎处附有红色或白色血栓, 并且没有消化道其他部位出血的证据. 还可以通过临床表现来辅助判断出血: 呕血、黑

■背景资料

食管静脉曲张出血是导致肝硬化患者死亡的主要原因, 内镜套扎术是首选的治疗方法. 然而套扎术后的再出血率仍很高, 如何预防再出血引起了广泛关注.

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■ 研发前沿

套扎术后再出血的预防性治疗方法较多,单独或联合治疗的效果不一,总结分析以上治疗方法的疗效,有助于完善目前预防性治疗的策略。

便、心率加快、血压下降以及积极输血后血红蛋白无明显升高或下降。

套扎术1986年由研究者^[1-3]提出,被广泛应用于食管静脉曲张出血的治疗,其对再出血的预防治疗作用在多项研究中得到证实。有研究表明,套扎环数多的患者早期再出血率高,原因可能有两点:首先,需要套扎的曲张静脉数目多,对应的有出血征象的血管就多,这间接反映了门脉压力高以及将来再出血的可能性大;更重要的是,多点套扎使受损伤黏膜和套扎后溃疡的面积增大,也增加了再出血的风险。该研究中再出血患者中,由于套扎后溃疡引起的出血占到58.3%^[1]。同样,在Petrasc等^[2]的研究中,套扎后溃疡引起的再出血也占到46.7%。由此可见,积极预防或治疗套扎术后溃疡对于预防再出血至关重要,尤其是对于套扎环数较多的患者。红色征常作为预测静脉曲张出血风险的可靠指标,Okamoto等^[3]的研究指出,重度静脉曲张患者食管下段右后壁的红色征最明显,而破裂出血最常发生于右前壁,可能与此处血管跨壁压最大有关。因此在进行初次套扎治疗时,无论食管下段右前壁的红色征是否明显都应对其进行结扎。

2 二次预防治疗

2.1 内镜及手术预防 首次套扎的早期再出血率为7.8%^[4],2年的再出血率为27%-34%^[5,6]。由于初次套扎后的再出血率高,因此在初次止血成功后,要通过药物或内镜治疗来预防再次出血。然而,这些措施仅能显著降低再出血率却不能降低死亡率^[7]。

通过反复套扎达到根除曲张静脉来有效预防再出血的研究,已在多项试验^[7-9]中开展。与硬化术相比能显著改善再出血率,与药物预防相比^[7]能减少严重并发症的发生。然而,上述试验的套扎治疗间期却各不相同。关于适宜的套扎治疗间期,仅有一项回顾性研究,表明预防性套扎的治疗间期长于3 wk可明显降低再出血率^[9]。由于是回顾性的研究,这一结论的可靠性有限,还需要更多随机对照研究证实。

关于套扎术后易于再出血的时间, Lee等^[1]的研究表明,入院2 wk内的再出血率最高。另一回顾性研究指出,急诊套扎患者的再出血多发生于11 d内,而择期套扎患者的再出血多发生于4 d内^[2]。同样, Xu等^[4]的研究显示,套扎后的早期出血80.8%发生于7-13 d内。由此可见,套扎术后再出血的高峰期是在2 wk内,在此期间应注意积

极防护,避免再出血的发生,尤其是对于合并有肝硬化其他并发症的患者。

对于肝功Child A级和B级的食管静脉曲张出血的患者^[10],若合并胃底静脉曲张,其再出血的风险是单纯食管静脉曲张患者的4倍。该试验表明应用电凝法治疗套扎术后的微小曲张静脉是安全有效的,电凝后无一例发生再出血,而应用注射法的患者中有8.3%出现再出血,但注射法的优势是静脉曲张的再发生率低。

一项Meta分析^[11]指出,预防再出血中联合应用套扎及硬化术并不能改善患者的预后,没有降低再出血率,也没有缩短静脉曲张消失所需要的治疗时间。同时,联合治疗时发生食管狭窄的风险明显增加。而另一Meta分析则认为联合治疗效果更优^[12]。Grgov等^[13]的研究表明,应用硬化术处理套扎后剩余的小曲张静脉并不能改善再出血率,还会增加吞咽困难及胸痛等并发症。因此,不推荐应用硬化治疗预防再出血。

Baveno V会议^[14]根据非对照研究结果推荐覆膜金属自膨胀支架可应用于难控制性静脉曲张的止血。难治性出血指经过药物和内镜治疗仍持续出血,不包括因大量出血妨碍内镜治疗的患者。在这种情况下,内镜支架成为可替代气囊填塞的另一选择^[15]。其可能的并发症如加重出血,食管纵膈穿孔,支架取出后再出血等,在多项研究^[16,17]中均未发生。在Zehetner等^[16]的研究中有7个患者支架脱落至胃中,但未引起再出血,并于48 h内成功将支架再次回放入食管。在另一研究^[17]中,3/9的患者止血失败,其中2例是胃溃疡,并且发生支架相关小溃疡1例,但未引起再出血。而Dechêne等^[5]的研究指出,虽然支架可以成功止血,但取出支架后仅应用保守治疗再出血率高,建议将支架作为应用其他治疗方法的过渡治疗。但由于该研究的病历数少,其统计学意义有限。上述研究中的支架放置时间1-14 d,但止血效果相似,可能跟研究的样本量少有关。因此,关于支架在急性止血中的作用还需要将来大量样本随机对照试验进行验证。

此外,经颈静脉肝内门体分流术^[18](transjugular intrahepatic portosystemic stent, TIPS)通过降低门静脉系统的压力来降低患者再出血的风险。TIPS与套扎相比^[6,19]能降低再出血率,但不能改善死亡率,还会增加患者发生肝性脑病以及形成门静脉血栓^[20]的风险,因此不推荐作为预防出血的首选治疗方法,可作为患者进行肝移植的过渡治疗,也可用于治疗难治性出血^[21-23]。选择

性分流术^[20]与完全分流术相比, 止血率相同, 但并发肝性脑病比例低, 为目前推荐的治疗方法. 选择性TIPS^[24]与静脉曲张硬化术相比能有效降低再出血率及死亡率, 并且二者诱发肝性脑病的比率相同. 肝移植是终末期肝病的选择, 并不适用于预防出血的治疗.

2.2 药物预防 一项关于雷贝拉唑服用2年的随机对照试验^[25]表明, 长期服用质子泵抑制剂能显著降低静脉曲张出血率及套扎相关的严重并发症, 但并不能降低静脉曲张的再发生率. 因此, 单独应用质子泵抑制剂不能明显改善肝硬化出血患者的预后, 还需要联合其他治疗方法.

门静脉压力梯度(hepatic venous pressure gradient, HVPG) >12 mmHg^[26-28]预示患者静脉曲张出血的风险增加, 非选择性 β 受体阻滞剂被普遍应用于降低HVPG, 以降低再出血率. 最近的一项前瞻性研究^[7]表明, 持续使用非选择性 β 受体阻滞剂预防首次出血和再出血的患者, 与未预防用药的患者相比, 其套扎后的远期再出血率和死亡率都增加. 提示我们对这类患者应采用套扎的替代治疗, 以改变这一结局. 另一研究^[29]指出, 止血成功后大剂量使用 β 受体阻滞剂能改善患者6 wk内的再出血率及死亡率. 这一结论在多项研究^[30-33]中得到证实. 一项Meta分析^[34]表明, 应用 β 受体阻滞剂与套扎预防再出血的效果相同. 而Kumar等^[35]及Ahmad等^[36]的研究指出预防性应用 β 受体阻滞剂并不能降低再出血率. 因此, 关于 β 受体阻滞剂能否降低再出血率仍存争议, 需要随机对照试验的验证. 单独应用非选择性 β 受体阻滞剂^[37]的患者应答率低, 即不能使HVPG降至12 mmHg以下, 或比基础值降低小于20%, 联合应用哌唑嗪能显著改善其应答率, 但并不能降低再出血率. 此外, 套扎术是 β 受体阻滞剂应答率低患者预防止血的可行方法^[38].

3 预防并发症

多项随机对照实验研究了引起食管静脉曲张再出血的独立危险因素, 包括较差的Child-pugh分数^[39]或分级^[2,4,40,41]、 β 受体阻滞剂的应用^[7]及剂量^[25]、输血^[42-44]、血肌酐水平^[43,44]、血胆红素水平^[43,44]、感染^[1,39]、低白蛋白血症^[6,39,42]、HVPG ≥ 18 mmHg^[6,45]、腹水^[4,6]、肝癌^[8]、凝血酶原时间^[4] >18 s及套扎环数^[4]等. 由于研究方法及指标不同, 研究所得再出血的独立影响因素也各不相同. 但如果患者同时有上述多项危险因素, 则预示其再出血可能性大. 在总的死亡事件中, 出血

所引起的只占到34.2%, 大多数的死亡由肝硬化的其他并发症引起^[46]. 因此预防这些并发症对于改善肝硬化患者的预后十分重要. 感染是评估急性食管静脉曲张出血患者早期再出血及死亡率可靠指标. 除出血外, 感染^[47-49]所致的败血症是患者早期死亡的另一主要原因, 肠内需氧的革兰阴性菌是肝硬化静脉曲张患者最常见的致病菌^[1]. 目前推荐^[50]肝硬化出血患者入院即开始使用抗生素, 并持续使用7 d, 具体抗生素的选择可依据当地微生物的耐药情况^[51]来选择. 同时还应避免应用肾毒性药物如氨基糖苷类和非甾体抗炎药, 并应避免低血容量以减少对肾功的损害. 肝硬化患者经常合并营养失调, 因此一旦患者病情稳定应积极经口进食. 此外, 肝功衰竭是套扎患者死亡的主要原因, 因此预防和治疗肝功衰竭是改善患者生存率的主要方法.

4 结论

肝硬化患者出血的诱因是多方面的, 其治疗也要综合其各项指标选择最合适的治疗方法. 随着人们对这一并发症的认识及治疗水平不断提高, 以及对可能的并发症及预后的准确评估, 有助于降低肝硬化的发生率.

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■相关报道

Augustin等认为, 套扎术后再出血病情复杂, 需要多学科协作, 选取最优方案, 建议尽早应用血管活性药物, 随后根据情况采取补救治疗措施: 包括内镜、气囊、食道支架、断流或分流手术等.

■应用要点

套扎术后再出血问题已得到临床重视,但尚未形成统一的治疗方案,预防性治疗的方法多样,对最新的研究成果进行总结有助于指导临床选择最有效的治疗方案。

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■同行评价

本文结合近年来的文献,总结了食管静脉曲张套扎后再出血发生的原因、预防手段和治疗进展,对临床有一定指导意义。

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