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导管接触性溶栓同期球囊扩张 + 支架治疗血栓性髂静脉压迫综合征的疗效*

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摘要 目的:为提高治疗效率,本研究对髂静脉压迫综合征合并下肢深静脉血栓患者的导管接触溶栓同期球囊扩张 + 支架治疗方案和分期治疗方案进行比较。**方法:**以 65 例髂静脉压迫综合征合并下肢深静脉血栓患者为研究对象,根据治疗方法分为研究组和对照组,研究组 32 例,进行导管接触溶栓同期球囊扩张 + 支架治疗,对照组 33 例,进行导管接触溶栓分期球囊扩张 + 支架治疗。以治疗前后患者大腿围、小腿围、血管通畅评分,手术指标(住院时间、住院次数、溶栓时间及穿刺次数),并发症(血栓复发、出血以及肺栓塞)及深静脉血栓后遗症为指标,考察两组疗效。**结果:**两组患者大腿围、小腿围和静脉通畅评分在治疗前均无显著差异($P>0.05$),经过治疗,两组大腿围、小腿围和静脉通畅评分均显著改善($P<0.05$),但两组间各项指标无显著差异($P>0.05$)。研究组患者住院时间、住院次数、溶栓时间及穿刺次数均显著低于对照组($P<0.05$)。研究组血栓复发 0 例,对照组血栓复发 4 例,有显著差异($P<0.05$);研究组出血 1 例,肺栓塞 0 例,对照组出血 2 例,肺栓塞 0 例,两组出血和肺栓塞情况比较,无显著差异($P>0.05$)。研究组 PTS 发生率为 6.25%,显著低于对照组的 18.18%($P<0.05$)。**结论:**导管接触溶栓同期球囊扩张 + 支架治疗方案对髂静脉压迫综合征合并下肢深静脉血栓有良好的疗效。

关键词:导管接触溶栓;球囊扩张;支架;髂静脉压迫综合征;下肢深静脉血栓

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The Effect of Catheter Contact Thrombolysis with Balloon Expansion and Stent in the Treatment of Thrombotic Iliac Vein Compression Syndrome*

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ABSTRACT Objective: In order to improve the efficiency of treatment, this study compared catheter contact thrombolysis in patients with iliac vein compression syndrome and deep vein thrombosis at the same time as balloon dilatation + stent treatment plan and staged treatment plan. **Methods:** Sixty-five patients with iliac vein compression syndrome combined with deep vein thrombosis of the lower extremities were taken as the research objects. According to the treatment method, they were divided into study group and control group. Thirty-two patients in the study group received catheter-contact thrombolysis and balloon dilatation + stent therapy at the same time; 33 patients in the control group received catheter-contact thrombolysis and balloon dilatation + stent therapy. The patient's thigh circumference, calf circumference, vascular patency score, surgical indicators (hospitalization time, hospitalization times, thrombolysis time and puncture times), complications (thrombosis recurrence, bleeding, and pulmonary embolism) and sequelae of deep vein thrombosis are used as indicators. **Results:** The thigh circumference, calf circumference and venous patency scores of the two groups of patients were not significantly different before treatment ($P>0.05$). After treatment, the thigh circumference, calf circumference and venous patency scores of the two groups were significantly improved ($P<0.05$). There was no significant difference in various indicators between the two ($P>0.05$). The length of hospitalization, the number of hospitalizations, the time of thrombolysis and the number of punctures in the study group were significantly lower than those in the control group ($P<0.05$). There were 0 cases of thrombosis recurrence in the study group and 4 cases of thrombosis recurrence in the control group ($P<0.05$). There were 1 bleeding in the study group, 0 pulmonary embolism, 2 bleeding in the control group, and 0 pulmonary embolism. There was no significant difference in bleeding and pulmonary embolism between the two groups ($P>0.05$). The incidence of PTS in the study group was 6.25%, which was significantly lower than 18.18% in the control group ($P<0.05$). **Conclusion:** Catheter contact thrombolysis at the same time balloon dilatation + stent treatment program has a good effect on iliac vein compression syndrome with deep vein thrombosis of lower limbs.

Key words: Catheter contact thrombolysis; Balloon expansion; Stent; Iliac vein compression syndrome; Deep vein thrombosis of the lower extremities

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前言

髂静脉压迫综合征 (Iliac vein compression syndrome, IVCS) 是由各种原因引起的髂静脉受压, 导致受压侧下肢与盆腔发生的一系列以血液回流障碍为主要表现的症状和体征, 多伴有下肢深静脉血栓形成 (Deep venous thrombosis, DVT)^[1], DVT 指的是血液在深静脉管腔内发生异常凝固, 使血液回流受阻, 进而引发下肢肿胀疼痛、色素沉着、溃疡、慢性静脉功能不全等一系列症状, 且进行性加重, 治疗后易复发^[2]。如不进行及时有效的治疗, 随着血栓逐渐机化, 以及瓣膜被其破坏, 易转变为慢性静脉功能不全, 被称为深静脉血栓后遗症 (post-thrombosis syndrome, PTS), 甚至是致死性肺栓塞 (Pulmonary embolism, PE)^[3]。

传统治疗方法多采用手术取栓、单纯抗凝以及系统溶栓等, 临床疗效及安全性均难以令人满意, 无法预防 PE, 远期 PTS 发生率较高^[4]。对伴有 DVT 的 IVCS, 去除血栓的同时对髂静脉病变也进行处理是治疗且降低后遗症的关键。近年来, 血管腔内介入基础逐渐发展、成熟, 导管接触溶栓 (catheter-directed thrombolysis, CDT) 被中华医学会外科学分会推荐为 DVT 治疗的一线策略^[5]。但其置管时间长、有出血风险, CDT 结合球囊成形以及支架植入术已经称为血栓性 IVCS 的主要治疗手段, 具有对患处定位准确, 患者创伤小、恢复快等优点, 在保证消除 DVT 的同时, 也解除了髂静脉的狭窄、闭塞情况, 降低了血栓复发率^[6]。为提高治疗效率, 本研究对 IVCS 合并 DVT 患者的导管接触溶栓同期球囊扩张 + 支架治疗方案和分期治疗方案进行比较, 具体如下。

1 研究对象

1.1 基本信息

以 2018 年 4 月 ~2020 年 5 月就诊于我院的 IVCS 合并 DVT 患者为研究对象, 根据治疗方法分为研究组和对照组, 研究组 32 例, 进行导管接触溶栓同期球囊扩张 + 支架治疗, 男性 13 例, 女性 19 例, 年龄 32~82 岁, 平均 (54.8 ± 15.3) 岁, 病程 2~14 d, 平均 (5.1 ± 3.3) d。中央型 9 例, 混合型 23 例。对照组 33 例, 进行导管接触溶栓分期球囊扩张 + 支架治疗, 男性 13 例, 女性 20 例, 年龄 31~82 岁, 平均 (55.2 ± 16.7) 岁, 病程 2~13 d, 平均 (4.8 ± 4.3) d。中央型 11 例, 混合型 22 例。两组患者基本信息如性别构成比、年龄、病程等经分析无统计学意义 ($P > 0.05$), 具有可比性。患者及家属均充分了解研究内容并签署知情同意书, 本研究已获得医院伦理委员会的准许。

1.2 纳入与排除标准

纳入标准: 患者术前经血管超声以及下肢静脉造影检查明确诊断者; 为初次发生的 DVT, 且病程 ≤ 14 d; 为中央型或混合型 DVT; ≤ 85 岁; 溶栓后经造影确认有髂静脉闭塞或明显受压情况 (狭窄 > 70%), 且存在侧支循环, 造影剂延迟排空等情况。

排除标准: 有抗凝、溶栓禁忌者, 如严重的内脏活动性出血、急性脑血管意外等; 心肺功能不全耐受差患者; 对造影剂有严重过敏反应者; 病程 > 14 d 的陈旧性 DVT; 伴有严重基础疾病者。

1.3 研究方法

两组患者均予入院后完善术前检查, 排除禁忌后, 进行手术治疗。其中研究组进行导管接触性溶栓同期球囊扩张 + 支架治疗: CDT 前为防止血栓脱落, 置入通用型下腔静脉滤器 (inferior vena caver filter, IVCF), 在数字减影血管造影 (digital subtraction angiography, DSA) 下采用 Seldinger 技术经健侧股静脉置入 5F 血管鞘, 鞘内造影明确下腔静脉 (IVC) 管径粗细, 了解有无血栓、畸形。明确双肾静脉开口, 在有肾静脉开口下 0.5~1 cm 处置入 IVCF。再进行 CDT 治疗, 依据血液学检查结果选择造影时机, 经造影确认血栓溶解后, 取出溶栓导管, 同期行髂静脉球囊扩张以及支架置入术。滤器置入 2~3 w 后经 DSA 造影明确有无捕获血栓, 没有血栓或血栓最大径 < 1 cm 则使用圈套器经回收鞘取出。对照组进行导管接触性溶栓分期球囊扩张 + 支架治疗, 先进行 IVCF 置入, 再进行 CDT 治疗, 依据血液学检查结果选择造影时机, 经造影确认血栓溶解后, 取出溶栓导管, 院外继续抗凝治疗, 于 2 w 行 IVCF 取出术, 再进行髂静脉球囊扩张 + 支架植入术。

导管接触性溶栓术: 患者取仰卧位, 进行常规消毒铺巾, 经局麻后从右股静脉穿刺造影, 再置入滤器, 确认滤器上缘低于肾静脉开口, 且高于髂静脉分叉位置。撤出鞘管加压包扎后取俯卧位, 重新进行消毒、铺巾, 在超声引导下进行左腘静脉穿刺, 根据造影结果, 确认血栓位置、长度, 再置入溶栓导管并留置。经溶栓导管进行溶栓治疗, 以 60 万 ~80 万 U/d 剂量尿激酶持续泵入 48 h, 并给予低分子肝素抗凝治疗。每 12 h 进行血常规及 D-二聚体水平检测, 根据纤维蛋白原水平调整尿激酶用量, 当肿胀明显缓解后, 进行造影以明确血栓溶解情况。

髂静脉球囊扩张 + 支架置入术: 取俯卧位, 消毒铺巾, 经原左腘静脉穿刺入路, 沿导丝插入球囊扩张导管至髂静脉狭窄段进行球囊扩张, 经过充分扩张后, 在髂静脉狭窄段置入 COOK 静脉支架, 支架的直径为 14~16 mm, 长度为 60~140 mm。支架植入后将滤器取出, 经造影确认支架形状良好, 完全覆盖病变部位, 无造影剂外渗情况, 下腔静脉血流通畅。

两组患者术后均口服抗凝药物, 口服华法林者, 目标 INR 控制在 2.0~3.0; 口服利伐沙班者, 前 3 w 15 mg, 2 次/d, 3 w 后调整为 20 mg, 1 次/d, 治疗 3~6 个月, 根据复查结果调整用量。

1.4 观察指标

分别于治疗前后测量患者大腿围、小腿围, 大腿围测量部位为患肢髌骨上 15 cm 处, 小腿围测量部位为患肢髌骨下缘 10 cm 处。进行血管通畅评分^[7], 依次对下腔、髂总、髂外、股总、近端股浅、远端股浅和腘静脉部位进行评分, 完全堵塞为 2 分, 部分堵塞为 1 分, 完全通畅为 0 分, 各项评分总分即为血管通畅评分。

详细统计每位患者治疗期间有关参数, 如住院时间、住院次数、溶栓时间及穿刺次数等。距离患者治疗中出现的并发症如血栓复发、出血以及肺栓塞等。

治疗后 6 个月复查, 记录 Villalta^[8]评分, 对患肢肿胀、皮肤瘙痒、静脉性肌肉挛缩等 5 项症状和水肿、浅静脉曲张、色素沉着、皮炎等 6 项体征进行评分, 根据从无到重, 评分记为 0~3 分, 计算总分, 评分 > 5, 则诊断为 PTS。

1.5 数据处理

以 SPSS 19.0 对数据进行分析, 计量资料以 $\bar{x} \pm s$ 表示, 使

用 t 检验,计数资料采用率(%)表示,计量资料使用 χ^2 检验, $P < 0.05$ 为具有统计学意义。

2 结果

2.1 近期疗效

本研究对两组近期疗效进行比较,结果见表 1,两组患者大腿围、小腿围和静脉畅通评分在治疗前均无显著差异 ($P > 0.05$),经过治疗,两组大腿围、小腿围和静脉畅通评分均显著改善 ($P < 0.05$),但两组间各项指标无显著差异 ($P > 0.05$)。

表 1 两组近期疗效比较

Table 1 Comparison of short-term efficacy between the two groups

Groups	Thigh circumference /cm		Calf circumference /cm		Venous patency score	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group (n=32)	44.91± 5.45	40.31± 4.21*	36.45± 3.91	34.23± 3.21*	6.24± 1.21	0.61± 0.36*
Control group(n=33)	45.28± 4.01	41.30± 2.76*	37.30± 2.76	34.30± 2.15*	6.25± 1.55	0.71± 0.34*

Note: * $P < 0.05$ compared with before treatment.

2.2 住院时间、住院次数、溶栓时间及穿刺次数

本研究对两组患者住院时间、住院次数、溶栓时间及穿刺

次数进行比较,结果见表 2 所示,研究组患者住院时间、住院次数、溶栓时间及穿刺次数均显著低于对照组 ($P < 0.05$)。

表 2 两组手术指标比较

Table 2 Comparison of surgical indicators between the two groups

Groups	Hospitalization time/day	Number of hospitalizations	Thrombolysis time/day	Number of punctures
Study group (n=32)	10.15± 2.19*	1.00± 0.00*	7.13± 2.13*	3.01± 0.15*
Control group(n=33)	13.76± 1.62	2.34± 0.43	9.24± 2.14	3.82± 0.23

Note: * $P < 0.05$ compared with control group.

2.3 治疗后并发症及 PTS 发生情况比较

本研究对治疗后并发症及 PTS 发生情况进行比较,结果表明,研究组血栓复发 0 例,对照组血栓复发 4 例,有显著差异 ($P < 0.05$);研究组出血 1 例,肺栓塞 0 例,对照组出血 2 例,肺

栓塞 0 例,两组出血和肺栓塞情况比较,无显著差异 ($P > 0.05$)。研究组 PTS 发生率为 6.25%,显著低于对照组的 18.18% ($P < 0.05$),结果见表 3 所示。

表 3 治疗后并发症及 PTS 发生情况比较(例,%)

Table 3 Comparison of complications and PTS occurrence after treatment (n,%)

Groups	Thrombosis recurrence	Bleeding	Pulmonary embolism	PTS
Study group (n=32)	0(0.00)	1(3.12)	0(0.00)	2(6.25)
Control group(n=33)	4(12.12)*	2(6.06)	0(0.00)	6(18.18)*

Note: * $P < 0.05$, compared with control group.

3 讨论

对于单纯的髂静脉受压,若没有临床症状,临床上通常不采取治疗措施。当患者伴有下肢慢性肿胀、静脉曲张、色素沉着、等下肢慢性静脉功能不全的表现时,需要进行干预^[9,10]。根据是否有血栓的形成将 IVCS 分为两类:非血栓性 IVCS 和血栓性 IVCS^[10,11]。临床研究表明,反复的髂静脉受压能增加下肢深静脉血栓的发病率^[12,13]。因此对于血栓性 IVCS 应早诊断早治疗。治疗的首要目的是清除血栓梗塞,减小下肢静脉压力,降低对静脉瓣的破坏,进而减少远期 PTS 和 DVT 的发生率。腔内介入技术日益成熟,如置管溶栓治疗、球囊扩张治疗、支架置入治疗,有成功率高、创伤小以及并发症相对较少等优势,已称为 IVCS 的首选治疗方式^[14,15]。

CDT 采用血管穿刺及导丝引导,使溶栓管放置于血栓处,持续泵入尿激酶等溶栓药物。其中,尿激酶能通过刺激纤溶酶原生成纤溶酶使血栓溶解,能保证药物与血栓的充分接触^[16,17]。相较于静脉滴注,减少了血液对药物的稀释,有效减少肝脏代谢,降低了药物的并发症,一般溶栓 48 h 即可使大部分血栓溶解,侧枝循环血液回流恢复^[18]。CDT 治疗中所用到的导丝、导管等器械易引起血栓的脱落导致肺栓塞,需在介入前必要放置下腔静脉滤器^[19,20]。髂静脉球囊扩张及支架置入时机目前有一定的分歧。治疗中,髂静脉先行球囊扩张,若扩张后髂静脉弹性回缩高于 50%则应置入髂静脉支架^[21]。单纯的球囊扩张能短暂的恢复髂静脉正常管径,但数据表明两年内下腔静脉血栓复发率高达 47%~73%^[22]。为降低再发生狭窄闭塞发生率,保证髂静脉的长期通畅,本研究创新性采用导管接触溶栓同期球囊扩张

+ 支架治疗方案对髂静脉压迫综合征合并下肢深静脉血栓患者进行治疗,并分期治疗方案进行比较,对两组近期疗效进行比较,结果表明,两组患者大腿围、小腿围和静脉通畅评分在治疗前均无显著差异,经过治疗,两组大腿围、小腿围和静脉通畅评分均显著改善,但两组间各项指标无显著差异。

Schaefer JK^[23]研究认为,髂静脉受压能作为天然屏障,阻止大体积的血栓通过,能降低溶栓过程中血栓的脱落,较分期治疗中引发致死性肺栓塞的概率小;Olinger CR^[24]研究表明髂静脉受压也能使溶栓过程中药物与血栓的接触时间增加,提高血栓溶解效果。本研究使用 CDT 对血栓性 IVCS 患者进行治疗,清除血栓后对患者进行髂静脉造影,并同期行髂静脉球囊扩张以及支架植入,对两组患者住院时间、住院次数、溶栓时间及穿刺次数进行比较,结果表明,研究组患者住院时间、住院次数、溶栓时间及穿刺次数均显著低于对照组。与上述学者研究结果有所不同,本研究中同期行髂静脉球囊扩张以及支架植入术,能增加髂静脉血流流速增加,有利于减少血栓的负荷量,加速患者恢复。其原因在于,同期治疗能减少血栓的负荷量,使血流快速恢复,有效减少平均住院时间,降低整体治疗的费用,而单纯的 CDT 需要更多的溶栓时间,使住院时间延长,增加了患者的经济负担^[25]。

本研究对治疗后并发症及 PTS 发生情况进行比较,结果表明,研究组血栓复发 0 例,对照组血栓复发 4 例,有显著差异;研究组出血 1 例,肺栓塞 0 例,对照组出血 2 例,肺栓塞 0 例,两组出血和肺栓塞情况比较,无显著差异。研究组 PTS 发生率为 6.25%,显著低于对照组的 18.18%。在髂静脉压迫综合征合并下肢深静脉血栓的治疗中,导管接触溶栓同期球囊扩张+支架治疗方案能尽早的清除血栓,改善症状,尽快恢复流入道和流出道血流速度,且很大程度上保护了静脉瓣膜功能,从而降低了 PTS 发生率。对于髂静脉压迫综合征合并下肢深静脉血栓患者,抗凝治疗能有效抑制血栓的蔓延,需贯穿于整个治疗过程的始终^[26,27]。手术中的球囊扩张及支架置入操作对血管内膜有一定的刺激或损伤,为了有效的防止血栓再发,患者有必要进行长期的抗凝治疗,虽然抗凝时间越长发生再阻塞的概率越低,但患者的出血概率随之增加,根据临床经验,建议口服华法林抗凝 4-6 个月^[28-30]。

综上所述,导管接触溶栓同期球囊扩张+支架治疗方案对髂静脉压迫综合征合并下肢深静脉血栓有良好的疗效,能有效减少住院时间、住院次数、溶栓时间及穿刺次数,降低血栓复发及 PTS 发生率。

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