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• 临床研究 •

覆膜支架腔内修复术对 Stanford B 型主动脉夹层动脉瘤患者术后血清血管内皮生长因子、核因子- κ B 水平的影响*任 恺 李步滢 段维勋 俞 波 俞世强[△] 金振晓

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摘要 目的: 分析覆膜支架腔内修复术对 Stanford B 型主动脉夹层动脉瘤患者术后血清血管内皮生长因子 (VEGF)、核因子- κ B (NF- κ B) 水平的影响。**方法:** 选取 2015 年 6 月~2017 年 6 月空军军医大学第一附属医院收治的 150 例 Stanford B 型主动脉夹层动脉瘤患者, 根据治疗方法不同分为两组。对照组(75 例)采用药物治疗, 观察组(75 例)采用覆膜支架腔内修复术治疗, 对比两组治疗前后血清血管内皮生长因子(VEGF)、核因子- κ B(NF- κ B)、白细胞介素-1 β (IL-1 β)、干扰素- γ (IFN- γ)、急性生理和慢性健康状况 (Acute physiology and chronic health evaluation, APACHE II) 评分、SF-36 量表评分的变化, 并发生(内漏、动脉栓塞、左上肢乏力、支架后移等)发生情况, 再次手术或介入治疗发生率及病死率。**结果:** 治疗后, 观察组血清 VEGF、NF- κ B、IL-1 β 、IFN- γ 水平显著低于对照组($P<0.05$); 两组治疗后 APACHE II 评分均较治疗前降低, SF-36 量表评分均较治疗前升高, 且观察组 APACHE II 与 SF-36 量表评分改善程度大于对照组($P<0.05$); 观察组并发症总发生率 4%、再次手术或介入治疗发生率为 5.33%, 病死率为 1.33%, 均显著低于对照组(17.33%、21.33%、10.67%, $P<0.05$)。**结论:** 覆膜支架腔内修复术能显著提高 Stanford B 型主动脉夹层动脉瘤患者生活质量与生存率, 并发症与再治疗发生率, 改善其病情, 可能降低 VEGF、NF- κ B 水平有关。

关键词: Stanford B 型主动脉夹层动脉瘤; 血管内皮生长因子; 覆膜支架腔内修复术; 核因子- κ B

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Effect of Endovascular Stent-graft repair on the Serum Vascular Endothelial Growth Factor and Nuclear Factor- κ B Levels in Patients with Stanford Type B Aortic Dissection*REN Kai, LI Bu-ying, DUAN Wei-xun, YU Bo, YU Shi-qiang[△], JIN Zhen-xiao

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ABSTRACT Objective: To analyze the effects of endovascular stent-graft repair on serum vascular endothelial growth factor (VEGF) and nuclear factor-kappaB (NF- κ B) levels in patients with Stanford type B aortic dissection. **Methods:** A total of 150 Stanford type B aortic dissection aneurysms admitted to the First Affiliated Hospital of Air Force Military Medical University from June 2015 to June 2017 were divided into two groups according to different treatment methods. The control group (75 cases) was treated with drugs, and the observation group (75 cases) was treated with stent-graft endovascular repair. Serum vascular endothelial growth factor (VEGF) and nuclear factor-KB (NF- κ B) were compared before and after treatment. Interleukin-1 β (IL-1 β), interferon- γ (IFN- γ), acute physiology and chronic health evaluation (APACHE II) score, SF-36 scale score change, the complication (endoleak, arterial embolism, left upper limb weakness, stent displacement, etc.), the incidence and mortality of reoperation or interventional therapy. **Results:** After treatment, the levels of serum VEGF, NF- κ B, IL-1 β and IFN- γ in the observation group were significantly lower than those in the control group ($P<0.05$). The APACHE II scores in the two groups were lower than those before treatment, and the amount of SF-36 was decreased. Table scores were higher than those before treatment, and the improvement of APACHE II and SF-36 scales in the observation group was greater than that in the control group ($P<0.05$). The total incidence rate of complications in the observation group was 4%, and the incidence of reoperation or interventional treatment rate was 5.33%, the case fatality rate was 1.33%, which was significantly lower than those of the control group (17.33%, 21.33%, 10.67%, $P<0.05$). **Conclusion:** Intraluminal prosthesis can significantly improve the quality of life and survival rate as well as complications and retreatment rates of patients with Stanford type B aortic dissection aneurysm, besides, improve their condition, which may be related to the reduction of VEGF and NF- κ B levels.

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Key words: Stanford type B aortic dissection aneurysm; Vascular endothelial growth factor; Endovascular repair with stent graft; Nuclear factor- κ B

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前言

主动脉夹层也称为主动脉夹层动脉瘤,是由多种原因引发主动脉壁内膜破裂,血液进入主动脉中膜而发生主动脉真假两腔分离性病变,根据 Stanford 法分型,未累及升主动脉病变为 Stanford B 型主动脉夹层动脉瘤^[1]。药物与介入腔内手术是治疗 Stanford B 型主动脉夹层动脉瘤常用方法,其中药物可较快控制患者血压和左心室射血速度,降低疾病危险程度,介入腔内手术可修复主动脉腔,降低并发症发生风险,但临床对治疗方式选择尚存在一定争议^[2]。部分研究提示对病情稳定 Stanford B 型主动脉夹层动脉瘤尤其是主动脉壁内血肿患者应采用保守治疗,但药物治疗过程中可能转归为典型主动脉夹层瘤;腔内修复术通过覆膜支架对近端破口进行覆盖封闭,仅解决了夹层主要问题,其所致并发症情况尚需深入探究^[3]。鉴于此,本研究选取了 150 例 Stanford B 型主动脉夹层动脉瘤患者,探讨了覆膜支架腔内修复术的临床应用价值,结果报道如下。

1 资料和方法

1.1 一般资料

选取 2015 年 6 月~2017 年 6 月空军军医大学第一附属医院收治的 150 例 Stanford B 型主动脉夹层动脉瘤患者,根据治疗方法不同分组。其中,观察组 75 例,男 50 例,女 25 例,年龄 33~76 岁,平均(52.66 ± 9.83)岁,致病原因:61 例伴有高血压,10 例伴有动脉粥样硬化,4 例由外伤致病;对照组 75 例,男 47 例,女 28 例,年龄 35~75 岁,平均(53.20 ± 9.10)岁,致病原因:63 例伴有高血压,6 例伴有动脉粥样硬化,6 例由外伤致病。两组性别、年龄、致病原因等资料均衡可比($P > 0.05$)。本研究符合《世界医学会赫尔辛基宣言》相关要求。

1.2 纳入标准及排除标准

(1)纳入标准:均根据病史、临床症状、血流动力学检查、实验室检查确诊;签署知情同意书;首次发病;未合并恶性肿瘤;无颅内其他病变。(2)排除标准:Stanford A 型主动脉夹层瘤手术治疗后发生的 Stanford B 型主动脉夹层动脉瘤;既往有覆膜支架植入史;存在相关药物过敏史者;无法正常沟通交流者;凝血功能障碍者。

1.3 治疗方法

(1)对照组:采用药物治疗,于重症监护病房接受治疗,绝对卧床,监测生命体征,给予镇痛、镇静、通便、止咳、负性肌力药物治疗,并给予硝普钠、乌拉地尔、美托洛尔、硝酸甘油等静脉滴注,心电监护下保守治疗 2 周以上,控制心率($60 \sim 100$ 次/min)与血压($100 \sim 120$ mmHg),观察有无胸痛等症状缓解;保持血压、心率平稳;观察胸腔积液有无增加;复查血管增强 CT 观察主动脉夹层有无进展、主动脉夹层假腔变化等。(2)观察组:采用覆膜支架腔内修复术治疗,术前均给予药物保守治疗,方法同对照组,病情稳定后开展手术,术前 1d 晚上禁食,取平卧位,在数

字减影(DSA)监视下完成,应用 Seldinger 穿刺技术经左肘窝区左肱动脉搏动处穿刺,19gauge 动脉穿刺针穿刺,置入并保留 0.035 导丝,撤去穿刺针,顺导丝置入 5F 导管鞘,拔除鞘管、导丝内芯,冲洗鞘管。辅以 5F 黄金标记猪尾导管,置 5F 肱动脉动脉鞘入升主动脉,行正位、左前斜 $40^\circ \sim 50^\circ$ 位 DSA 造影,掌握真假腔位置、病变位置、夹层内膜破口位置、角度与累及范围,测量破口近端相对正常主动脉内径、破口与左锁骨下动脉距离、瘤体最大直径,根据造影和测量结果确定支架直径和长度,参考术前 DSA,入路位置选择髂外动脉无明显扭曲且未受累一侧,做斜行腹股沟切口,显露股动脉,穿刺后置入 6F 导管鞘,经鞘置入 6F 猪尾巴管,交换为超硬导丝,沿导丝送覆膜支架至预定位置,控制心率约 90 次/min,收缩压约 90 mmHg,透视下释放支架,再次造影明确支架位置,判断是否通畅及发生内漏,缝合股动脉与切口,加压包扎穿刺位置,患者病情稳定返回重症监护病房。

1.4 观察指标

(1)治疗前后采集空腹静脉血,分离血清,以酶联免疫法测定血清核因子- κ B(NF- κ B)、血管内皮生长因子(VEGF)、白细胞介素-1 β (IL-1 β)、干扰素- γ (IFN- γ)水平。(2)治疗前后综合病情采用急性生理和慢性健康状况评分(Acute physiology and chronic health evaluation, APACHE II 评分)评价,生存质量采用 SF-36 量表评价。(3)随访 1 年,统计并发症(内漏、动脉栓塞、左上肢乏力、支架后移等)的发生情况、再次手术或介入治疗发生率、病死率。

1.5 统计学方法

采用 SPSS20.0 统计学软件处理数据,计量资料以($\bar{x} \pm s$)表示,组间比较采用 t 检验,计数资料用[例(%)]表示,组间比较采用 χ^2 检验,以 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 两组手术情况的比较

观察组 75 例 Stanford B 型主动脉夹层动脉瘤患者覆膜支架腔内修复术均获成功,术后即刻主动脉造影显示无支架变形与移位。

2.2 两组治疗前后血清 NF- κ B、VEGF、IL-1 β 、IFN- γ 水平的比较

治疗前,两组血清 VEGF、NF- κ B、IL-1 β 、IFN- γ 水平比较无显著差异($P > 0.05$);治疗后,观察组血清 VEGF、NF- κ B、IL-1 β 、IFN- γ 水平均显著低于对照组($P < 0.05$)。见表 1。

2.3 两组治疗前后 APACHE II 与 SF-36 量表评分的比较

治疗前,两组 APACHE II 与 SF-36 量表评分比较无显著差异($P > 0.05$);治疗后,两组 APACHE II 评分均较治疗前降低, SF-36 量表评分均较治疗前升高,且观察组 APACHE II 与 SF-36 量表评分改善程度大于对照组($P < 0.05$)。见表 2。

2.4 两组随访情况的比较

随访 1 年,两组无病例脱落现象发生。观察组并发症总发

表 1 两组血清 VEGF、NF- κ B、IL-1 β 、INF 水平的比较($\bar{x}\pm s$)Table 1 Comparison of the serum VEGF, NF- κ B, IL-1 β , INF levels between the two groups before and after treatment($\bar{x}\pm s$)

Time	Groups	Case	VEGF(PB/ML)	NF- κ B(mmoL/L)	IL-1 β (ng/L)	INF- γ (ng/L)
Before treatment	Observation group	75	1.14 $\pm$ 0.07	0.97 $\pm$ 0.10	3.82 $\pm$ 1.02	2.36 $\pm$ 0.49
	Control group	75	1.13 $\pm$ 0.08	0.98 $\pm$ 0.12	3.79 $\pm$ 1.12	2.40 $\pm$ 0.51
	t		0.815	0.554	0.172	0.490
	P		0.417	0.580	0.864	0.625
After treatment	Observation group	75	0.51 $\pm$ 0.06	0.62 $\pm$ 0.13	1.55 $\pm$ 0.25	0.48 $\pm$ 0.26
	Control group	75	0.82 $\pm$ 0.07	0.71 $\pm$ 0.11	2.18 $\pm$ 0.46	1.33 $\pm$ 0.20
	t		29.119	4.577	10.421	22.441
	P		0.000	0.000	0.000	0.000

表 2 两组治疗前后 APACHE II 与 SF-36 量表评分的比较($\bar{x}\pm s$, 分)Table 2 Comparison of the APACHE II and SF-36 scale scores between the two groups before and after treatment ($\bar{x}\pm s$, score)

Groups	Case	APACHE II Score		t	P	SF-36 scale score		t	P
		Before treatment	After treatment			Before treatment	After treatment		
Observation group	75	43.33 $\pm$ 8.26	6.61 $\pm$ 3.19	35.914	0.000	42.17 $\pm$ 11.06	86.69 $\pm$ 6.88	29.601	0.000
Control group	75	42.09 $\pm$ 7.98	15.78 $\pm$ 4.65	24.670	0.000	43.88 $\pm$ 15.71	72.18 $\pm$ 7.59	14.047	0.000
t		0.935	14.083			0.771	12.267		
P		0.351	0.000			0.442	0.000		

生率为 4%、再次手术或介入治疗发生率为 5.33%、病死率为 0.05)。见表 3。
1.33%，均分别显著低于对照组 (17.33%、21.33%、10.67%， $P<$

表 3 两组随访情况的比较[例(%)]

Table 3 Comparison of the follow-up between the two groups[n(%)]

Groups	Case	Complications					The incidence of		Mortality rate
		Small amount of endoleak	Brain infarction	Arterial embolization	Left upper limb weakness	Liver and kidney dysfunction	Total incidence	reoperation or interventional therapy	
Observation group	75	1(1.33)	0(0)	1(1.33)	1(1.33)	0(0)	3(4.00)	4(5.33)	1(1.33)
Control group	75	0(0)	7(9.33)	0(0)	0(0)	6(8.00)	13(17.33)	16(21.33)	8(10.67)
χ^2							6.996	8.308	4.255
P							0.008	0.004	0.039

3 讨论

Stanford B 型主动脉夹层动脉瘤是心血管一种急危重症，具有起病急骤、进展迅速特点，急性起病 12h 内病死率高达 33.3%，及早诊治对促进病情转归意义重大^[4,5]。药物治疗目标是维持动脉收缩压在 100~120 mmHg，心率等于或稍低于患病前，降低左心室收缩力，减轻血流搏动对主动脉壁冲击，以防止夹层进一步破裂或撕裂^[6-8]。既往研究显示药物治疗稳定型 Stanford B 型主动脉夹层动脉瘤患者五年生存率为 86%^[9-11]，但持续血流灌注假腔与夹层动脉瘤不断扩张可导致相关并发症发生，常需再次手术干预。孟庆友等^[12]研究显示药物治疗后再次手术或介入治疗发生率为 20%，本研究中对对照组再次手术或介入治疗发生率为 21.33%，与以上学者研究结果相似，提示单

一依赖药物治疗后存在较大比例患者需再次手术或介入治疗，因此临床对于符合介入手术治疗指征患者常给予腔内修复术治疗。

覆膜支架腔内修复术是由 Dake 在 1994 年首先描述应用的，为治疗 Stanford B 型主动脉夹层动脉瘤提供了新思路，其具有创伤小、恢复快等优点，临床应用较为广泛^[13-15]。陶然等^[16]研究显示 Stanford B 型主动脉夹层腔内修复术后患者胸主动脉假腔明显缩小，真腔明显扩大，腹部重要分支动脉供血得到改善。本研究中，观察组 75 例 Stanford B 型主动脉夹层动脉瘤患者覆膜支架腔内修复术均获成功，真腔明显扩大，与以上学者一致。Shintani T 等^[17]报道对 1 名 66 岁患者进行 2 年随访，发现其术后 2 年 CT 扫描提示 B 型主动脉夹层支架移植物移位。本研究术后即刻主动脉造影显示无支架变形与移位，提示

手术成功,术后1年随访无支架移位发生,与以上学者结果存在差异,可能与术后随访时间较短有关。且本研究在以上研究基础上发现覆膜支架腔内修复术能降低Stanford B型主动脉夹层动脉瘤患者并发症与再次手术或介入治疗发生率,提高患者生存率。覆膜支架腔内修复术通过大血管覆膜支架对近心端主动脉夹层第一破口进行覆盖,终止第一破口入假腔内血流,促使假腔内自上而下形成血栓而被吸收,降低动脉夹层瘤破裂风险,减少残留假腔远期病变发生,且能恢复真腔血流,扩张真腔,提高内脏血管血流,重建主动脉结构,恢复其正常生理功能,故可改善患者预后^[18,19]。

既往研究表明 VEGF 可促进血管内皮细胞迁移和细胞外基质变性^[20-23];NF- κ B 可调控炎症因子表达,直接或间接作用于微血管内皮细胞,导致微循环障碍^[24,25];IL-1 β 是一种炎症因子,参与血管水肿及组织损伤过程^[26-28];IFN- γ 能导致平滑肌细胞凋亡^[29,30]。而本研究结果显示观察组治疗后血清 VEGF、NF- κ B、IL-1 β 、IFN- γ 水平低于对照组,说明覆膜支架腔内修复术能改善Stanford B型主动脉夹层动脉瘤患者机体炎症反应,保护动脉血管,这可能是覆膜支架腔内修复术除修复术自身外的另一作用机制,从侧面反映抑制炎症反应与血管新生可能有助于Stanford B型主动脉夹层动脉瘤的治疗,为临床应用药物保守治疗Stanford B型主动脉夹层动脉瘤提供了新思路。此外,观察组治疗后APACHE II与SF-36量表评分改善程度大于对照组,说明覆膜支架腔内修复术可更有效改善患者的病情,提高患者的生活质量。

综上所述,膜支架腔内修复术能显著提高Stanford B型主动脉夹层动脉瘤患者生活质量与生存率并发症与再治疗发生率,改善其病情,可能与游戏降低VEGF、NF- κ B水平有关。

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