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覆膜支架腔内修复术与药物保守治疗对 Stanford B 型主动脉夹层动脉瘤患者肝肾功能、炎症因子以及预后的影响*

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摘要 目的:比较覆膜支架腔内修复术与药物保守治疗对 Stanford B 型主动脉夹层动脉瘤的疗效及对患者肝肾功能、炎症因子及预后的影响。**方法:**选择 2012 年 1 月~2014 年 8 月我院收治的 Stanford B 型主动脉夹层动脉瘤患者 68 例,按照随机数字表法分为对照组与研究组,各 34 例。对照组入院后采取药物保守治疗,研究组应用覆膜支架腔内修复术治疗。观察两组住院期间死亡率、再次手术或介入率以及治疗前、治疗 2 周后肝肾功能、血清炎症因子变化。所有患者随访 36 个月,比较两组患者预后情况。**结果:**研究组再次手术或介入率为 2.94%,低于对照组的 22.58% ($P<0.05$)。治疗 2 周后,研究组丙氨酸转氨酶(ALT)、天门冬氨酸氨基转移酶(AST)、尿素氮(BUN)、肌酐(Cr)、胱抑素 C、肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β)、 γ -干扰素(INF- γ)、C 反应蛋白(CRP)水平较治疗前降低($P<0.05$),且研究组低于对照组($P<0.05$)。两组患者均随访 36 个月,随访 12 个月时两组患者生存率分别为 100.00%和 80.65%,随访 36 个月时两组患者生存率分别为 91.18%和 29.03%,经 Log Rank 分析显示,两组生存率比较差异有统计学意义($P<0.05$)。**结论:**覆膜支架腔内修复术治疗 Stanford B 型主动脉夹层动脉瘤的疗效确切,能够改善患者肝肾功能,降低炎症反应,患者近中期随访生存率较高,其效果优于保守治疗。

关键词:覆膜支架腔内修复术;保守治疗;Stanford B 型;主动脉夹层动脉瘤;肝功能

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Effect of Endovascular Repair of Covered Stent and Drug Conservative Treatment on Liver and Renal Function, Inflammatory Factors and Prognosis in Patients with Stanford B Aortic Dissecting Aneurysm*

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ABSTRACT Objective: To compare the effect of endovascular repair of covered stent and drug conservative treatment on Stanford B aortic dissecting aneurysm and its effects on liver and renal function, inflammatory factors and prognosis. **Methods:** 68 patients with Stanford B aortic dissecting aneurysm who were admitted to our hospital from January 2012 to August 2014 were selected, the patients were divided into the control group and the study group according to the random number table method, 34 cases in each group. The control group was treated with drug conservative treatment after admission, the study group was treated with endovascular repair of covered stent. The mortality, reoperation or intervention rate of the two groups during hospitalization and the changes of liver and renal function and serum inflammatory factors before treatment and 2 weeks after treatment were observed. All patients were followed up for 36 months, and the prognosis of the two groups was compared. **Results:** The rate of reoperation or intervention of the study group was 2.94%, which was lower than 22.58% of the control group ($P<0.05$). At 2 weeks after treatment, the alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea nitrogen (BUN), creatinine (Cr), Cystatin C, tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interferon- γ (INF- γ) and C reactive protein (CRP) levels in the study group were lower than before treatment ($P<0.05$), and the study group was lower than that of the control group ($P<0.05$). The two groups were followed up for 36 months, and the survival rates of the two groups were 100.00% and 80.65% at 12 months of follow-up respectively, the survival rates of the two groups were 91.18% and 29.03% at 36 months of follow-up respectively. Log Rank analysis showed that there was a significant difference in the survival rate of the two groups ($P<0.05$). **Conclusion:** The treatment of Stanford B aortic dissecting aneurysm with membrane covered stent repair has effect, it can improve the liver and renal function and reduce the inflammatory response, the survival rate of the patients is higher in the middle period, and the effect is better than that of the conservative treatment.

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前言

主动脉夹层动脉瘤是临床上较为少见的危重心血管病变,其发病率约为 5~10/100 万,该病病情发展迅速,死亡率较高^[1]。目前临床上通常根据病变累及范围将主动脉夹层动脉瘤分为 Stanford A 型(主动脉夹层累及升主动脉及其远端)、Stanford B 型(主动脉夹层累及左锁骨下动脉远端主动脉)^[2,3]。Stanford B 型是主动脉夹层动脉瘤的常见类型,药物保守治疗、介入治疗和手术治疗是目前 Stanford B 型主动脉夹层动脉瘤的常用治疗方法^[4,5]。外科手术治疗由于创伤较大,围手术期死亡率较高,通常用于急性发病阶段^[6]。上世纪末覆膜支架腔内修复术成功应用于临床,该方法具有创伤小、术后并发症发生率低等优点,已逐步取代了传统外科手术治疗。有研究表明,肾功能不全不是 Stanford B 型主动脉夹层动脉瘤患者死亡的独立危险因素^[7],另外炎症反应也会加重主动脉夹层动脉瘤的进展,导致治疗失败^[8]。本研究通过对比分析覆膜支架腔内修复术与药物保守治疗对 Stanford B 型主动脉夹层动脉瘤患者肝肾功能、炎症因子及预后的影响,旨在为 Stanford B 型主动脉夹层动脉瘤治疗方案的选择提供依据。

1 资料与方法

1.1 一般资料

选择 2012 年 1 月~2014 年 8 月我院收治的 Stanford B 型主动脉夹层动脉瘤患者 68 例,纳入标准:(1)所有患者均符合主动脉夹层动脉瘤的诊断标准^[9],入院急诊经动脉 CT 血管造影诊断确诊为 Stanford B 型主动脉夹层动脉瘤;(2)发病时间 ≤ 14 d;(3)累及左锁骨下动脉远端主动脉至股动脉;(4)患者病历资料完整;(5)患者及家属已知晓本次研究,并签署知情同意书。排除标准:(1)合并非典型主动脉夹层、外伤等其他主动脉疾病;(2)累及肾动脉者;(3)合并其他感染性疾病、慢性消耗性疾病;(4)入院时已存在肝肾功能不全;(5)随访过程中失访的患者。将入选患者按照随机数字表法分为对照组与研究组。对照组 34 例,男 19 例,女 15 例;年龄 32~61 岁,平均年龄(46.64 \pm 6.63)岁;合并高血压 11 例、合并糖尿病 12 例;夹层血管直径 35~58 mm,平均(46.33 \pm 5.74) mm。研究组 34 例,男 17 例,女 17 例;年龄 30~59 岁,平均年龄(45.87 \pm 6.98)岁;合并高血压 12 例、合并糖尿病 11 例;夹层血管直径 38~59 mm,平均(47.12 \pm 5.32) mm。研究组与对照组患者一般资料经统计分析差异无统计学意义($P>0.05$)。本研究经医院伦理委员会同意。

1.2 方法

两组患者入院后均行急诊主动脉 CTA 检查,对照组入院后立即给予严格控制血压、控制心率、镇痛、镇静等治疗,包括降压、维持水电解质平衡、镇痛、镇静、调整营养、给予钙离子拮抗剂、 β 受体阻滞剂等。研究组在夹层发生后 2 周给予覆膜支架腔内修复术治疗,期间给予保守治疗,方案同对照组。方法如下:(1)术前评估:术前完善各项检查,行急诊动脉 CT 血管造

影进行全动脉评估,了解动脉瘤位置、破口数量、大小、夹层血管直径等,双侧股动脉直径,夹层有无累及等,根据测量结果选择合适的支架,支架直径选择以超过测量动脉口径 10%~15% 为宜。(2)手术方法:患者在局麻下进行手术,首先给予肝素 5000 U,经左侧肱动脉穿刺送入导管至升主动脉,经右侧股动脉送入导丝至升主动脉位置,将覆膜支架沿导丝送入病变部位。将患者血压控制在 100 mmHg 左右,松开覆膜支架,随后在造影下观察支架的位置、形态、贴壁情况,缝合股动脉。将患者送入监护室,密切观察患者生命体征,术后常规应用抗生素抗感染治疗,并维持患者动脉收缩压在 120 mmHg 以下。

1.3 观察指标

(1)观察对比两组住院期间死亡率、再次手术或介入率。(2)分别于治疗前、治疗 2 周后采集患者清晨空腹外周静脉血 8 mL,离心(速率为 5000 r/min,半径为 6 cm)5 min,分离血清,应用 5300S 型全自动生化分析仪检测患者的肝功能。主要包括:丙氨酸转氨酶(ALT)、天门冬氨酸氨基转移酶(AST)等指标。应用速尿法和酶法检测两组患者的肾功能,主要包括:尿素氮(BUN)、肌酐(Cr)和胱抑素 C。(3)应用酶联免疫吸附法测定两组患者的血清炎症因子,主要包括:肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β)、 γ -干扰素(INF- γ)、C 反应蛋白(CRP)水平,试剂盒购自 BIO RAD 公司,严格按照试剂盒操作说明进行。(4)所有患者随访 36 个月,观察两组患者预后情况。

1.4 统计学处理

应用 SPSS20.0 分析数据。以率(%)表示住院期间死亡率、再次手术或介入率等计数资料,采用 χ^2 检验。以($\bar{x}\pm s$)表示肝功能指标、炎症因子指标等计量资料,采用 t 检验。此外,建立 Kaplan-Meier 生存模型,并应用 Log Rank 检验分析两组生存率差异。 $P<0.05$ 表明差异有统计学意义。

2 结果

2.1 两组住院期间死亡率、再次手术或介入率比较

两组住院期间死亡率分别为 0.00%(0/34)和 8.82%(3/34),两组比较差异无统计学意义($P>0.05$)。两组再次手术或介入率分别为 2.94%(1/34)和 22.58%(7/31),研究组再次手术或介入率低于对照组($P<0.05$)。见表 1。

2.2 两组治疗前、治疗 2 周后肝肾功能比较

治疗前两组患者 ALT、AST、BUN、Cr、胱抑素 C 水平等 5 个指标比较差异无统计学意义($P>0.05$)。治疗 2 周后,对照组各指标与治疗前比较差异无统计学意义($P>0.05$),研究组的 ALT、AST、BUN、Cr、胱抑素 C 水平较治疗前均明显下降($P<0.05$),且治疗 2 周后研究组以上各指标水平低于对照组($P<0.05$)。见表 2。

2.3 两组治疗前、治疗 2 周后血清炎症因子比较

治疗前两组患者血清 TNF- α 、IL-1 β 、INF- γ 、CRP 水平比较差异无统计学意义($P>0.05$)。治疗 2 周后,对照组各指标与治

疗前比较差异无统计学意义 ($P>0.05$), 研究组血清 TNF- α 、2 周后研究组以上各指标水平低于对照组 ($P<0.05$)。见表 3。
IL-1 β 、INF- γ 、CRP 水平较治疗前均明显下降 ($P<0.05$), 且治疗

表 1 两组住院期间死亡率、再次手术或介入率比较[n(%)]

Table 1 Comparison of mortality during hospitalization, reoperation or intervention rate of two groups[n(%)]

Groups	n	Mortality during hospitalization	Reoperation or intervention rate
Study group	34	0(0.00)	1(2.94)
Control group	34	3(8.82)	7(22.58)*
χ^2		1.395	4.118
P		0.238	0.042

Note: * reoperation or intervention rate was calculated after deducting the number of deaths.

表 2 两组治疗前后肝肾功能比较($\bar{x}\pm s$)

Table 2 Comparison of liver and kidney functions between the two groups before and after treatment($\bar{x}\pm s$)

Groups	ALT(U/L)		AST(U/L)		BUN(mmol/L)		Cr(mmol/L)		Cystatin C(mg/L)	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Study group (n=34)	46.72 \pm 12.87	30.12 \pm 5.67*	56.28 \pm 15.33	31.12 \pm 6.11*	7.82 \pm 2.12	6.24 \pm 1.89*	123.1 \pm 17.86	95.12 \pm 12.73*	1.12 \pm 0.23	0.93 \pm 0.18*
Control group (n=31)	45.45 \pm 11.45	46.25 \pm 12.44	57.12 \pm 14.78	58.64 \pm 15.32	7.78 \pm 2.14	7.83 \pm 1.92	122.4 \pm 17.22	125.6 \pm 19.06	1.13 \pm 0.25	1.12 \pm 0.22
t	0.419	6.826	0.224	9.671	0.076	3.362	0.161	7.643	0.168	3.825
P	0.677	0.000	0.823	0.000	0.940	0.001	0.873	0.000	0.867	0.000

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

表 3 两组治疗前后血清炎症因子比较($\bar{x}\pm s$)

Table 3 Comparison of serum inflammatory factors between the two groups before and after treatment($\bar{x}\pm s$)

Groups	TNF- α (ng/mL)		IL-1 β (ng/mL)		INF- γ (ng/mL)		CRP(ng/mL)	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Study group (n=34)	52.34 \pm 12.44	28.12 \pm 8.97*	4.22 \pm 0.67	2.12 \pm 0.45*	3.14 \pm 0.72	1.76 \pm 0.56*	17.92 \pm 3.94	8.12 \pm 2.56*
Control group (n=31)	50.65 \pm 14.23	52.26 \pm 17.53	4.18 \pm 0.64	4.23 \pm 0.76	3.17 \pm 0.76	3.19 \pm 0.78	17.88 \pm 3.86	17.34 \pm 2.88
t	0.511	7.081	0.246	13.763	0.163	8.546	0.041	13.664
P	0.611	0.000	0.806	0.000	0.871	0.000	0.967	0.000

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

2.4 两组患者预后情况比较

两组患者均随访至 36 个月。随访 12 个月时研究组和对照组两组患者生存率分别为 100.00%和 80.65%, 随访 36 个月时两组患者生存率分别为 91.18%和 29.03%。两组 Kaplan-Meier 生存曲线见图 1。经 Log Rank 检验, 两组生存率比较差异有统计学意义($\chi^2=6.400, P=0.011$)。

3 讨论

目前临床上根据有无并发症, 常将 Stanford B 型主动脉夹层动脉瘤分为稳定性 Stanford B 型主动脉夹层动脉瘤和复杂

性 Stanford B 型主动脉夹层动脉瘤, 前者通常适用于药物保守治疗, 但有小部分患者在治疗过程中会出现并发症导致治疗失败^[10-12]。相关研究报道显示, 经过保守药物治疗可以阻止夹层破裂, 减轻病变部位血流冲击的压力, 但患者住院期间死亡率仍高达 10%以上^[13]。上世纪末覆膜支架腔内修复术在临床上应用取得了成功, 目前该术式已成为治疗 Stanford B 型主动脉夹层动脉瘤的常用方法。相关研究显示, Stanford B 型主动脉夹层动脉瘤患者经覆膜支架腔内修复术治疗后可以有效避免动脉夹层破裂, 降低病死率^[14]。但以往大部分研究旨在考察覆膜支架腔内修复术治疗 Stanford B 型主动脉夹层动脉瘤临床疗

效^[15,16],而关于该术式的随访研究并不多见。

本研究通过对我院收治的 Stanford B 型主动脉夹层动脉瘤患者 68 例对照研究发现,经保守治疗患者住院期间死亡率为 8.82%,同时有 22.58%的保守治疗患者由于出现无法控制高血压、持续发作的疼痛、主动脉扩张等并发症手术或介入治疗。而研究组住院期间未出现死亡,再次手术或介入率也低于对照组,表明覆膜支架腔内修复术治疗 Stanford B 型主动脉夹层动脉瘤死亡风险低。两组患者均随访 36 个月,从随访情况来看,随访 12 个月时两组患者生存率分别为 100%和 80.65%,随访 36 个月时两组患者生存率分别为 91.18%和 29.03%,经 Log Rank 分析显示,两组生存率比较有统计学差异。表明覆膜支架腔内修复术治疗 Stanford B 型主动脉夹层动脉瘤患者近、中期生存率优于保守治疗。分析原因主要是覆膜支架腔内修复术可以修补夹层部位,有效的降低了夹层破裂的高风险,而保守治疗虽然可以控制夹层破裂与管腔扩大,减轻血流动力学对动脉管壁的压力,但由于病变没有从根本上解除,因此仍有破裂的风险^[17,18]。保守治疗疗效不及覆膜支架腔内修复术可能还与保守治疗需长期服药、患者难以坚持、依从性较差等将影响治疗效果有关^[19,20]。

目前研究表明肝肾功能不全是 Stanford B 型主动脉夹层动脉瘤患者死亡的独立危险因素^[21]。而炎症反应也会加重主动脉夹层动脉瘤的进展,导致治疗难度增加^[22]。本研究显示,治疗后研究组患者 ALT、AST、BUN、Cr、胱抑素 C 水平较治疗前降低,对照组患者治疗前后 ALT、AST、BUN、Cr、胱抑素 C 水平无统计学差异,治疗后,与对照组比较,研究组患者肝肾功能指标水平降低。表明经过覆膜支架腔内修复术治疗后患者肝肾功能优于保守治疗患者。这可能是由于经过覆膜支架腔内修复术治疗后患者肝脏、肾脏等组织缺血得到缓解,血流动力学得到纠正,因此患者肝肾功能得到恢复^[23,24]。TNF- α 是一种有巨噬细胞产生的细胞因子,可以介导机体免疫反应,也是炎症反应的主要介质之一^[25]。IL-1 β 主要在 T 淋巴细胞和巨噬细胞中表达,在细胞壁和细胞基质成分破坏中起到重要作用^[26,27]。而 INF- γ 可以介导平滑肌细胞凋亡,在血管内皮细胞损伤中起到重要作用^[28]。CRP 属于急性主动脉夹层非特异性且敏感的炎症标记物,其也是预防心血管风险的独立危险因素^[29,30]。本研究结果显示,治疗后研究组患者血清 TNF- α 、IL-1 β 、INF- γ 、CRP 水平较治疗前降低,对照组患者治疗前后血清 TNF- α 、IL-1 β 、INF- γ 、CRP 水平无统计学差异,治疗后,与对照组比较,研究组患者血清炎性因子水平降低。表明经过覆膜支架腔内修复术治疗后患者体内炎症因子水平降低,而保守治疗后患者炎症因子水平并未发生明显变化,炎症反应仍持续存在,这可能是影响患者近中期生存率的重要因素,但其具体机制有待于进一步研究证实。

综上所述,保守治疗需长期服药,患者难以坚持,依从性较差,而覆膜支架腔内修复术治疗 Stanford B 型主动脉夹层动脉瘤可以有效避免动脉夹层破裂,且能降低患者肝肾功能,降低炎症反应,患者近中期随访生存率较高,效果优于保守治疗。

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