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论著·临床

术前血清 sCD163、sTWEAK 水平与 Stanford A 型主动脉夹层动脉瘤患者预后的关系

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【摘要】目的 分析术前血清可溶性血红蛋白清道夫受体(sCD163)、可溶性肿瘤坏死因子样凋亡弱诱导因子(sTWEAK)水平与 Stanford A 型主动脉夹层动脉瘤患者预后的关系。方法 选择 2016 年 1 月—2019 年 3 月河北医科大学第四医院心外科收治 Stanford A 型主动脉夹层动脉瘤患者 143 例作为观察组, 根据术后 3 年随访结果将患者分为存活亚组 115 例, 死亡亚组 28 例; 另选择同期医院体检健康者 140 例作为健康对照组。比较各组血清 sCD163、sTWEAK 水平; Pearson 法分析 Stanford A 型主动脉夹层动脉瘤患者术前血清 sCD163 与 sTWEAK 水平的相关性; Logistic 回归分析影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素; 受试者工作特征曲线(ROC)分析术前血清 sCD163、sTWEAK 对 Stanford A 型主动脉夹层动脉瘤患者死亡的预测价值。结果 死亡亚组高血压比例、术前血清低密度脂蛋白胆固醇(LDL-C)、心肌肌钙蛋白 I(cTnI)、D-二聚体(D-D)水平均显著高于存活亚组 [$\chi^2(t)/P = 4.481/0.034$ 、 $2.441/0.016$ 、 $2.181/0.031$ 、 $7.571/ < 0.001$]; 观察组术前血清 sCD163、sTWEAK 水平均显著高于健康对照组 ($t/P = 33.220/ < 0.001$ 、 $25.643/ < 0.001$); 死亡亚组术前血清 sCD163、sTWEAK 水平均显著高于存活亚组 ($t/P = 7.871/ < 0.001$ 、 $8.097/ < 0.001$); Stanford A 型主动脉夹层动脉瘤患者术前血清 sCD163 与 sTWEAK 水平呈正相关 ($r = 0.449$, $P < 0.001$); 术前 LDL-C、D-二聚体、sCD163、sTWEAK 水平升高是影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素 [$OR(95\% CI) = 3.066(2.125 \sim 4.423)$ 、 $2.090(1.215 \sim 3.596)$ 、 $2.396(1.381 \sim 4.156)$ 、 $2.979(2.183 \sim 4.064)$]; 术前血清 sCD163、sTWEAK 及二者联合预测 Stanford A 型主动脉夹层动脉瘤患者死亡的曲线下面积分别为 0.860、0.887、0.935, 二者联合预测效能高于单项预测 ($Z/P = 1.901/0.028$ 、 $2.331/0.019$)。结论 Stanford A 型主动脉夹层动脉瘤患者术前血清 sCD163、sTWEAK 水平升高, 是影响患者死亡的危险因素, 对患者死亡有一定预测价值。

【关键词】 主动脉夹层动脉瘤, Stanford A 型; 可溶性血红蛋白清道夫受体; 可溶性肿瘤坏死因子样凋亡弱诱导因子; 预后

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【Abstract】 Objective To analyze The relationship between preoperative serum soluble hemoglobin scavenger receptor (sCD163) and soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) and prognosis of patients with Stanford type A aortic dissection. Methods From January 2016 to March 2019, 143 patients with Stanford type A aortic dissecting aneurysm admitted to the Department of Cardiac Surgery of the Fourth Hospital of Hebei Medical University were selected as the observation group. According to the 3-year follow-up results, the patients were divided into 115 survival subgroups. 28 patients died in the subgroup; another 140 healthy people who underwent physical examination in the hospital during the same period were selected as the healthy control group. Comparison of serum sCD163 and sTWEAK levels in each group; Pearson analysis of the correlation between preoperative serum sCD163 and sTWEAK levels in patients with Stanford type A aortic dissection; Logistic regression analysis of the risk factors for death in patients with Stanford type A

aortic dissection; The predictive value of preoperative serum sCD163 and sTWEAK in patients with Stanford type A aortic dissecting aneurysm was analyzed by the operator operating characteristic curve (ROC). **Results** The proportion of hypertension, preoperative serum low-density lipoprotein cholesterol (LDL-C), cardiac troponin I (cTnI), and D-dimer levels in the death subgroup were significantly higher than those in the survival subgroup [$\chi^2(t)/P=4.481/0.034, 2.441/0.016, 2.181/0.031, 7.571/<0.001$]; the preoperative serum sCD163 and sTWEAK levels in the observation group were significantly higher than those in the healthy control group ($t/P=33.220/<0.001, 25.643/<0.001$); The preoperative serum sCD163 and sTWEAK levels in the group were significantly higher than those in survival subgroup ($t/P=7.871/<0.001, 8.097/<0.001$); preoperative serum sCD163 and sTWEAK levels in patients with Stanford type A aortic dissection were positively correlated ($r=0.449, P<0.001$); preoperative LDL C, D dimer, sCD163, and sTWEAK levels were the risk factors for death in patients with Stanford type A aortic dissection [$OR(95\%CI)=3.066(2.125-4.423), 2.090(1.215-3.596), 2.396(1.381-4.156), 2.979(2.183-4.064)$]; preoperative serum sCD163, sTWEAK and their combination predict the death of patients with Stanford type A aortic dissection under the curve The areas were 0.860, 0.887, and 0.935, respectively. The combined prediction efficiency of the two was higher than the single prediction ($Z/P=1.901/0.028, 2.331/0.019$). **Conclusion** Preoperative serum sCD163 and sTWEAK levels in patients with Stanford type A aortic dissecting aneurysm are elevated, which are risk factors for death and have certain predictive value for death.

【Key words】 Aortic dissection aneurysm, Stanford type A; Soluble hemoglobin scavenger receptor; Soluble tumor necrosis factor like weak inducer of apoptosis; Prognosis

Stanford A 型主动脉夹层动脉瘤是心血管疾病的危重症之一,若不及时治疗,易引发心力衰竭甚至死亡,早期评估其发生死亡的风险具有重要意义^[1-2]。可溶性血红蛋白清道夫受体(soluble hemoglobin scavenger receptor CD163, sCD163)可参与炎症反应,与心房颤动、冠状动脉粥样硬化病变程度及血管病变有关^[3-4]。吕忠俊等^[5]研究显示,血清 sCD163 水平升高,是下肢动脉硬化闭塞症患者介入术后再次狭窄独立危险因素。可溶性肿瘤坏死因子样凋亡弱诱导因子(soluble tumor necrosis factor like weak inducer of apoptosis, sTWEAK)参与炎症反应、氧化应激的过程,与冠状动脉病变程度有关^[6-7]。研究显示,血清 sTWEAK 水平升高与急性 ST 段抬高型心肌梗死(STEMI)患者经皮冠状动脉介入(PCI)术后发生心血管事件呈正相关^[8]。但血清 sCD163、sTWEAK 与 Stanford A 型主动脉夹层动脉瘤的相关性尚未有研究报道。现检测 Stanford A 型主动脉夹层动脉瘤患者血清 sCD163、sTWEAK 水平,并分析二者对患者预后的预测价值,报道如下。

1 资料与方法

1.1 临床资料 选择 2016 年 1 月—2019 年 3 月在河北医科大学第四医院心外科行手术治疗的 Stanford A 型主动脉夹层动脉瘤患者 143 例作为观察组,男 89 例,女 54 例,年龄 50~81(61.89 ± 9.50)岁。另选择医院同期体检健康者 140 例作为健康对照组,男 79 例,女 61 例,年龄 49~79(62.30 ± 9.70)岁。2 组性别、年龄比较差异无统计学意义($P>0.05$),具有可比

性。本研究经医院伦理委员会批准[LZS(2015)第 136 号],受试者及家属均知情同意并签署知情同意书。

1.2 病例选择标准 (1)纳入标准:①符合 Stanford A 型主动脉夹层动脉瘤诊断标准^[9];②经数字减影血管造影技术或 CT 血管造影确诊;③临床资料完整。(2)排除标准:①既往有主动脉夹层病史;②慢性肾功能不全者;③合并大动脉炎等血管疾病及恶性肿瘤患者。

1.3 观测指标与方法

1.3.1 临床资料收集:收集患者临床资料,包括性别、年龄、吸烟、饮酒、高血压病、冠心病、糖尿病史,术前白细胞计数(WBC)、血小板计数(PLT)、血红蛋白(Hb)、三酰甘油(TG)、总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、心肌钙蛋白 I(cTnI)、D-二聚体(D-D)、N 末端脑钠肽前体(NT-proBNP)、尿酸(UA)、总胆红素(TBil)等。

1.3.2 血清 sCD163、sTWEAK 水平检测:采集患者术前、健康者体检时空腹静脉血 5 ml,离心留取血清置于 -70°C 保存。以酶联免疫吸附法检测血清 sCD163、sTWEAK 水平,按 sCD163 试剂盒(上海起发实验试剂有限公司)、sTWEAK 试剂盒(上海臻科生物科技有限公司)说明书进行操作;采用酶标仪(型号 Varioskan LUX,美国赛默飞世尔科技公司)在 450 nm 波长处测 OD,通过绘制标准曲线计算出样品中 sCD163、sTWEAK 的水平。

1.3.3 预后随访:术后对 Stanford A 型主动脉夹层动脉瘤患者进行为期 3 年的随访(随访方式为门诊复查

或者电话),截至 2022 年 3 月 31 日,记录患者 3 年内死亡情况(全因死亡)。

1.4 统计学方法 采用 SPSS 25.0 软件进行数据统计分析。符合正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较行 t 检验;计数资料以频数或率(%)表示,组间比较采用 χ^2 检验;Pearson 法分析 Stanford A 型主动脉夹层动脉瘤患者术前血清 sCD163 与 sTWEAK 水平的相关性;Logistic 回归分析 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素;受试者工作特征曲线(ROC)分析术前血清 sCD163、sTWEAK 对 Stanford A 型主动脉夹层动脉瘤患者死亡的预测价值,曲线下面积(AUC)比较采用 Z 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 不同预后亚组患者临床资料比较 随访过程中无失访患者,存活 115 例(存活亚组),死亡 28 例(死亡亚组)。2 亚组患者性别、年龄、吸烟、饮酒、冠心病、糖尿病、WBC、PLT、Hb、TG、TC、HDL-C、NT-proBNP、UA、TBil 等比较差异无统计学意义($P > 0.05$);死亡亚组高血压比例、术前血清 LDL-C、cTnI、D-D 水平均显著高于存活亚组($P < 0.05$)。见表 1。

表 1 不同预后亚组患者临床资料比较

Tab.1 Comparison of clinical data of patients with different prognosis subgroups

项 目	存活亚组 ($n=115$)		死亡亚组 ($n=28$)		χ^2/t 值	P 值
男/女	73/42		16/12		0.385	0.535
年龄($\bar{x} \pm s$, 岁)	61.35 $\pm$ 9.42		64.10 $\pm$ 9.84		1.373	0.172
吸烟[例(%)]	48(41.74)		13(46.43)		0.202	0.653
饮酒[例(%)]	43(37.39)		9(32.14)		0.268	0.605
高血压[例(%)]	70(60.87)		23(82.14)		4.481	0.034
冠心病[例(%)]	41(35.65)		15(53.57)		3.035	0.081
糖尿病[例(%)]	44(38.26)		12(42.86)		0.200	0.655
WBC($\bar{x} \pm s$, $\times 10^9/L$)	10.47 $\pm$ 2.43	10.54 $\pm$ 2.21	0.139	0.890		
PLT($\bar{x} \pm s$, $\times 10^9/L$)	214.51 $\pm$ 40.98	218.61 $\pm$ 38.15	0.481	0.631		
Hb($\bar{x} \pm s$, g/L)	131.57 $\pm$ 19.48	132.65 $\pm$ 20.53	0.260	0.795		
TG($\bar{x} \pm s$, mmol/L)	1.27 $\pm$ 0.42	1.25 $\pm$ 0.38	0.230	0.818		
TC($\bar{x} \pm s$, mmol/L)	4.51 $\pm$ 0.83	4.61 $\pm$ 1.12	0.531	0.596		
HDL-C($\bar{x} \pm s$, mmol/L)	1.21 $\pm$ 0.23	1.15 $\pm$ 0.19	1.277	0.204		
LDL-C($\bar{x} \pm s$, mmol/L)	2.85 $\pm$ 0.90	3.31 $\pm$ 0.87	2.441	0.016		
cTnI($\bar{x} \pm s$, $\mu g/L$)	2.82 $\pm$ 0.91	3.24 $\pm$ 0.93	2.181	0.031		
D-D($\bar{x} \pm s$, $\mu g/L$)	1.32 $\pm$ 0.28	1.83 $\pm$ 0.45	7.571	<0.001		
NT-proBNP($\bar{x} \pm s$, ng/L)	842.23 $\pm$ 213.52	846.47 $\pm$ 220.36	0.094	0.926		
UA($\bar{x} \pm s$, $\mu mol/L$)	5.51 $\pm$ 1.24	5.61 $\pm$ 1.33	0.377	0.707		
TBil($\bar{x} \pm s$, $\mu mol/L$)	12.57 $\pm$ 2.34	12.65 $\pm$ 2.41	0.161	0.872		

2.2 2 组血清 sCD163、sTWEAK 水平比较 观察组术前血清 sCD163、sTWEAK 水平显著高于健康对照组

($P < 0.01$),见表 2。

表 2 健康对照组与观察组血清 sCD163、sTWEAK 水平比较 ($\bar{x} \pm s$)

Tab.2 Comparison of serum sCD163 and sTWEAK levels between healthy control group and observation group

组 别	例数	sCD163 ($\mu g/L$)	sTWEAK (ng/L)
健康对照组	140	9.36 $\pm$ 2.37	26.61 $\pm$ 7.23
观察组	143	28.55 $\pm$ 6.42	52.47 $\pm$ 9.55
t 值		33.220	25.643
P 值		<0.001	<0.001

注:sCD163.可溶性血红蛋白清道夫受体;sTWEAK.可溶性肿瘤坏死因子样凋亡弱诱导因子

2.3 不同预后亚组间血清 sCD163、sTWEAK 水平比较 死亡亚组术前血清 sCD163、sTWEAK 水平显著高于存活亚组($P < 0.01$),见表 3。

表 3 不同预后亚组间血清 sCD163、sTWEAK 水平比较 ($\bar{x} \pm s$)

Tab.3 Comparison of serum sCD163 and sTWEAK levels between different prognostic subgroups

组 别	例数	sCD163 ($\mu g/L$)	sTWEAK (ng/L)
存活亚组	115	26.42 $\pm$ 6.72	49.25 $\pm$ 8.86
死亡亚组	28	37.30 $\pm$ 5.83	65.69 $\pm$ 12.38
t 值		7.871	8.097
P 值		<0.001	<0.001

注:sCD163.可溶性血红蛋白清道夫受体;sTWEAK.可溶性肿瘤坏死因子样凋亡弱诱导因子

2.4 术前血清 sCD163、sTWEAK 水平的相关性分析 Pearson 分析结果显示,Stanford A 型主动脉夹层动脉瘤患者术前血清 sCD163 与 sTWEAK 水平呈正相关($r = 0.449, P < 0.001$)。

2.5 影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素分析 以是否发生死亡为因变量,是否患有高血压、术前 LDL-C、cTnI、D-D、sCD163、sTWEAK 为自变量,进行多因素 Logistic 回归分析显示,术前 LDL-C、D-D、sCD163、sTWEAK 水平升高是影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素($P < 0.05$),见表 4。

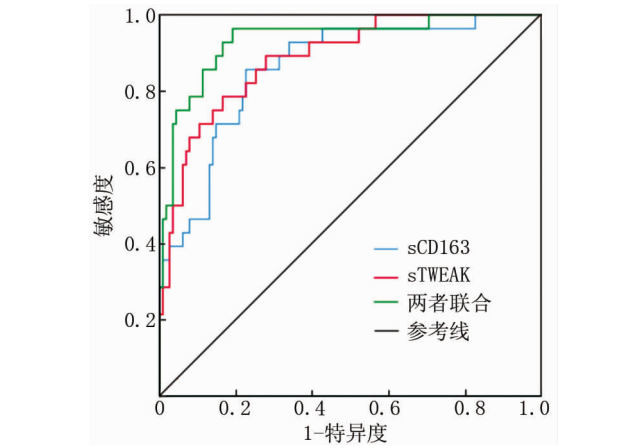
2.6 术前血清 sCD163、sTWEAK 对 Stanford A 型主动脉夹层动脉瘤患者死亡的预测价值 术前血清 sCD163、sTWEAK 及二者联合预测 Stanford A 型主动脉夹层动脉瘤患者死亡的 AUC 分别为 0.860、0.887、0.935,二者联合效能高于单项预测,差异有统计学意义($Z = 1.901、2.331, P = 0.028、0.019$),见图 1、表 5。

表 4 Stanford A 型主动脉夹层动脉瘤患者死亡的 Logistic 多因素分析

Tab. 4 Logistic multivariate analysis of death in patients with Stanford type A aortic dissecting aneurysm

因素	β 值	SE 值	Wald 值	P 值	OR 值	95% CI
有高血压	0.516	0.310	2.769	0.096	1.675	0.732 ~ 3.835
LDL-C 高	1.120	0.421	7.082	0.007	3.066	2.125 ~ 4.423
cTnI 高	0.639	0.383	2.785	0.095	1.895	0.895 ~ 4.012
D-D 高	0.737	0.305	5.842	0.004	2.090	1.215 ~ 3.596
sCD163 高	0.874	0.401	4.748	0.029	2.396	1.381 ~ 4.156
sTWEAK 高	1.088	0.423	6.623	0.010	2.979	2.183 ~ 4.064

注:sCD163. 可溶性血红蛋白清道夫受体;sTWEAK. 可溶性肿瘤坏死因子样凋亡诱导因子



注:sCD163. 可溶性血红蛋白清道夫受体;sTWEAK. 可溶性肿瘤坏死因子样凋亡诱导因子

图 1 术前血清 sCD163、sTWEAK 预测 Stanford A 型主动脉夹层动脉瘤患者死亡的 ROC 曲线

Fig. 1 ROC curve of preoperative serum sCD163 and sTWEAK in predicting death in patients with Stanford type A aortic dissecting aneurysm

表 5 术前血清 sCD163、sTWEAK 对 Stanford A 型主动脉夹层动脉瘤患者死亡的预测价值

Tab. 5 Preoperative serum sCD163 and sTWEAK in predictive value of death in patients with Stanford type A aortic dissecting aneurysm

指标	截断值	AUC	95% CI	敏感度	特异度	约登指数
血清 sCD163	31.45 $\mu\text{g/L}$	0.860	0.792 ~ 0.913	0.857	0.774	0.631
血清 sTWEAK	58.62 ng/L	0.887	0.823 ~ 0.934	0.786	0.835	0.621
二者联合	—	0.935	0.881 ~ 0.969	0.964	0.759	0.723

3 讨论

Stanford A 型主动脉夹层动脉瘤起病急,病情进展快且病情凶险,若治疗不及时 48 h 内病死率高达

50%,目前对于患者相关危险因素尚无确切结论,因此准确地评估患者病情,寻找预后不良危险因素,对降低患者病死率具有重要意义^[10-11]。Stanford A 型主动脉夹层动脉瘤的发病机制与动脉内皮功能障碍、粥样斑块破裂、炎症反应等因素密切相关^[12]。研究显示,高龄、外科手术、术前血小板计数偏低、低血压、D-D 水平升高、血脂水平升高等是影响 Stanford A 型主动脉夹层动脉瘤患者预后的危险因素^[13-14]。本研究结果显示,死亡亚组高血压患者比例、术前血清 LDL-C、cTnI、D-D 水平显著高于存活亚组,经 Logistic 回归分析显示,术前 LDL-C、D-D 水平升高为影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素,与以往报道结果类似。

sCD163 为血红蛋白清道夫受体,识别血红蛋白并结合珠蛋白形成复合体参与调控炎症反应^[15]。王朋妹等^[16]研究表明,急性呼吸窘迫综合征患者血清 sCD163 水平升高,sCD163 对病情评估及预后判断具有重要临床意义。另有研究显示^[17],冠状动脉粥样硬化(CAS)患者血清 sCD163 水平升高,并且与 CAS 病变程度及稳定性有一定相关性。sTWEAK 可作用于内皮细胞、平滑肌细胞等,与其特异性受体 Fn14 结合参与血管生成、内皮功能失调、炎症反应、斑块破裂等过程^[18]。研究显示^[19],STEMI 患者血清 sTWEAK 水平升高,是发生主要不良心血管事件的危险因素。本研究中,Stanford A 型主动脉夹层动脉瘤患者血清 sCD163、sTWEAK 水平升高,且二者呈正相关,提示二者共同参与疾病的发生,其可能的原因是 sCD163、sTWEAK 促进炎症反应,促进动脉粥样硬化致斑块破裂,引发主动脉夹层动脉瘤的发生。sTWEAK 可通过核转录因子等通路激活多种炎症因子,促进动脉粥样硬化的发展,还可促进基质金属蛋白酶(MMP)-2 和 MMP-9 的表达,影响斑块的稳定性^[20-21]。而 MMP-9 在动脉粥样硬化斑块内可发挥炎症细胞聚集的作用,还可激活明胶酶原,增加斑块不稳定性。

本研究还发现,死亡亚组患者血清 sCD163、sTWEAK 水平显著高于存活亚组,提示血清 sCD163、sTWEAK 水平变化与患者预后有关,Logistic 回归分析显示,术前血清 sCD163、sTWEAK 水平升高是影响 Stanford A 型主动脉夹层动脉瘤患者死亡的危险因素,提示血清 sCD163、sTWEAK 水平升高的患者有死亡的风险,可能成为潜在的预后标志物。本研究结果表明,血清 sCD163、sTWEAK 对于患者死亡有一定预测价值,但诊断效能不高,二者联合诊断具有较高的诊断效能,提示联合检测血清 sCD163、sTWEAK 水平对于预

测 Stanford A 型主动脉夹层动脉瘤患者预后有一定价值,在临床上对患者诊断与预后判断具有一定指导意义。

综上所述,Stanford A 型主动脉夹层动脉瘤患者血清 sCD163、sTWEAK 水平升高,是影响患者死亡的危险因素,二者联合对患者死亡有较高的预测价值,具有一定临床应用意义。

利益冲突:所有作者声明无利益冲突

作者贡献声明

崔荣敏:设计研究方案,实施研究过程,论文撰写;龚琪:提出研究思路,分析试验数据,论文审核;王哲:实施研究过程,资料搜集整理,论文修改;万翠翠:进行统计学分析

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