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## 替格瑞洛联合阿司匹林治疗老年急性冠状动脉综合征的效果 及对血清 cTnT、BNP、CRP 及 D-D 水平的影响\*

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**摘要 目的:**探讨替格瑞洛联合阿司匹林治疗老年急性冠状动脉综合征的效果及对血清肌钙蛋白-T(Cardiac Troponin T, cTnT)、C反应蛋白(C-reaction protein, CRP)、脑钠素(Brain natriuretic peptide, BNP)及 D-二聚体(D-Dimer, D-D)水平的影响。**方法:**选取 2016 年 1 月~2019 年 1 月我院收治的急性冠状动脉综合征老年患者 60 例,采用随机数字表法将患者分为两组,每组 30 例。两组患者均行经皮冠状动脉介入(Percutaneous coronary intervention, PCI)治疗,对照组术后给予阿司匹林和氯吡格雷,观察组给予阿司匹林和替格瑞洛。比较两组患者的临床治疗效果、心功能相关指标,治疗前后血清 cTnT、BNP、CRP 及 D-D 水平的变化情况以及出血事件的发生率。**结果:**治疗后,观察组治疗总有效率显著高于对照组(93.33% vs. 70%,  $P < 0.05$ );两组左室收缩末期内径(Left ventricular end systolic diameter, LVESD)、左室舒张末期内径(left ventricular end-diastolic diameter, LVEDD)、左心房内径(Left atrial diastolic diameter, LADD)、血清 cTnT、BNP、CRP 及 D-D 水平均较治疗前显著降低( $P < 0.05$ ),而左室射血分数(left ventricular ejection fraction, LVEF)较治疗前明显升高( $P < 0.05$ ),且观察组 LVESD、LVEDD、LADD 均明显低于对照组( $P < 0.05$ ),而 LVEF 显著高于对照组( $P < 0.05$ )。此外,观察组出血事件发生率显著低于对照组( $P < 0.05$ )。**结论:**与阿司匹林和氯吡格雷相比,替格瑞洛联合阿司匹林可更有效改善老年急性冠状动脉综合征患者的心功能,且出血事件的发生率更低,可能与其显著降低血清 cTnT、BNP、CRP 及 D-D 水平有关。

**关键词:**替格瑞洛;阿司匹林;老年急性冠状动脉综合征;效果

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## Efficacy of Ticagrelor Combined with Spirin in the Treatment of Elderly Patients with Acute Coronary Syndrome and Its Effect on the Serum cTnT, BNP, CRP and D-D Levels\*

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**ABSTRACT Objective:** To investigate the effect of ticagrelor combined with aspirin in the treatment of acute coronary syndrome in the elderly and on serum troponin-T (Catanic Troponin T, cTnT), C-reaction protein (CRP), brain natriuretic peptide (Brain natriuretic peptide, BNP) and D-dimer (D-D) levels. **Methods:** 60 cases of elderly patients with acute coronary syndrome admitted to our hospital from January 2016 to January 2019 were selected. The patients were divided into two groups using the random number table method, 30 cases in each group. Patients in both groups were treated with percutaneous coronary intervention (Percutaneous coronary intervention, PCI), while aspirin and clopidogrel were given postoperatively in the control group and aspirin and ticagrelor in the observation group. The clinical therapeutic effect, indicators related to cardiac function, serum cTnT, BNP, CRP and D-D levels before and after treatment and the incidence of bleeding events were compared between the two groups. **Results:** After treatment, the total effective rate in the observation group was significantly higher than that of the control group (93.33% vs. 70%,  $P < 0.05$ ). After treatment, left ventricular end systolic diameter (LVESD) and left ventricular end diastolic diameter (left Ventricular end-diastolic diameter (LVEDD), left atrial diastolic diameter (LADD), serum cTnT, BNP, CRP, and D-D levels were significantly lower than before treatment ( $P < 0.05$ ), while left ventricular ejection fraction (left The ventricular ejection fraction (LVEF) was significantly higher than that before treatment ( $P < 0.05$ ), and the LVESD, LVEDD, and LADD in the observation group were significantly lower than those in the control group ( $P < 0.05$ ), while the LVEF was significantly higher than the control group ( $P < 0.05$ ). The incidence of bleeding events was significantly lower than that in the control group ( $P < 0.05$ ). **Conclusion:** Compared with aspirin and clopidogrel, ticagrelor combined with aspirin is more effective in improving cardiac function in elderly patients with acute coronary syndrome, and the incidence of bleeding events is lower, which may significantly reduce serum cTnT, BNP, CRP and DD level related.

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## 前言

急性冠状动脉综合征(Acute coronary syndrome, ACS)是一组以冠状动脉硬化不稳定斑块破裂而继发冠脉血栓形成为病理基础的临床综合征,包括急性非 ST 段抬高型心肌梗死、急性 ST 段抬高型心肌梗死和不稳定性心绞痛<sup>[1-3]</sup>。近年来,随着人们生活水平的不断提高,ACS 的发病率呈现逐年上升的态势,且好发于老年男性和绝经后女性<sup>[4,5]</sup>。ACS 临床主要表现为胸痛、胸闷、呼吸困难等急性心肌缺血缺氧症状,严重影响患者的健康和生活质量,如不能得到及时有效的治疗会迅速进展为心肌梗死,甚至导致患者死亡,尤其是老年患者,已经成为冠心病患者的主要死亡原因<sup>[6-8]</sup>。PCI 是治疗 ACS 的有效方法,可重建患者的血运,但术后血栓形成是困扰临床治疗的主要问题<sup>[9,10]</sup>。

抗血小板聚集药物在预防术后血栓形成中具有重要作用,以往 ACS 患者的标准化双联抗血小板为阿司匹林和氯吡格雷,可显著降低患者的死亡率、支架内血栓和再发心肌梗死,但仍然有一部分患者由于存在阿司匹林和氯吡格雷抵抗而引起支架内血栓形成,所以需要寻找抗凝效果佳佳的药物进行 PCI 术后治疗<sup>[11-13]</sup>。替格瑞洛是一种新型的腺苷二磷酸受体拮抗剂,可快速强效的抑制血小板聚集<sup>[14,15]</sup>。因此,本研究主要探讨了替格瑞洛联合阿司匹林治疗老年急性冠状动脉综合征的效果及对患者血清 cTnT、BNP、CRP 及 D-D 水平的影响,现报道如下。

## 1 资料与方法

### 1.1 一般资料

选取 2016 年 1 月~2019 年 1 月我院收治的急性冠状动脉综合征老年患者 60 例,纳入标准:①符合中华医学会心血管病分会 ACS 指南中制定的相关诊断标准;②冠状动脉造影显示至少有 1 处狭窄需要行经皮冠状动脉介入治疗;③首次发病且发病时间在 12 h 内;④签署知情同意书。排除标准:①合并肝肾功能障碍者;②合并严重心功能不全及其他心血管疾病者;③合并中重度贫血、血小板减少及凝血功能异常者;④ 48 h 内接受过溶栓治疗者;⑤对本研究所用药物过敏者。采用随机数字表法将患者分为两组,对照组 30 例,男 18 例,女 12 例;年龄 60~75 岁;平均 65.32±3.25 岁;体质指数 21.85~16.37 kg/m<sup>2</sup>,平均 24.25±1.54 kg/m<sup>2</sup>;合并高血压 5 例,糖尿病 6 例,高脂血症 5 例。观察组 30 例,男 19 例,女 11 例;年龄 61~74 岁;平均

66.04±3.11 岁;体质指数 21.03~26.88 kg/m<sup>2</sup>,平均 24.85±1.47 kg/m<sup>2</sup>;合并高血压 6 例,糖尿病 7 例,高脂血症 4 例。两组一般基线资料比较差异均无统计学意义( $P>0.05$ ),具有可比性。

### 1.2 治疗方法

两组患者均给予纠正电解质平衡、抗凝、抗感染及抗血小板等常规治疗。术前给予阿司匹林肠溶片(甘肃祁连山药业股份有限公司,国药准字 H62021159) 150 mg,氯吡格雷片(赛诺菲(杭州)制药有限公司,国药准字 H20056410) 300 mg,服用后行 PCI 术,术后残余狭窄小于 10%为手术成功。对照组术后给予阿司匹林 100 mg/次,1 次/d,氯吡格雷 75 mg/次,1 次/d,连续服用 6 个月。观察组给予阿司匹林(服用方法同对照组)和替格瑞洛(深圳信立泰药业股份有限公司,国药准字 H20183320) 90 mg,2 次/d,连续服用 6 个月。

### 1.3 观察指标

① 临床治疗效果。② 心功能相关指标:于治疗前后采用彩色多普勒超声诊断仪对两组患者进行静息状态下心脏超声检查,LVESD、LVEDD、LADD,并计算 LVEF。③ 血清 cTnT、BNP、CRP 及 D-D 水平:分别于治疗前后抽取两组患者的空腹静脉血 5 mL,静置离心后分离血清,采用酶联免疫分析法测定 CRP 水平,采用化学发光法测定 cTnT、BNP 水平,采用免疫比浊法测定 D-D 水平。④ 出血事件发生率。

### 1.4 临床疗效评定标准

显效:患者的临床症状完全消失,心电图 T 波倒置和 ST 段压低基本恢复正常;有效:患者的临床症状明显改善,T 波倒置变浅 50%以上,ST 段压低部分改善。无效:未达到以上标准。

### 1.5 统计学方法

采用 SPSS16.0 对数据进行统计学分析,定性资料以%表示,组间比较行卡方检验,定量资料以( $\bar{x}\pm s$ )表示,组间比较行 t 检验,以  $P<0.05$  为有统计学差异。

## 2 结果

### 2.1 两组临床总有效率的比较

治疗后,观察组治疗总有效率显著高于对照组(93.33% vs. 70%, $P<0.05$ ),见表 1。

### 2.2 两组患者治疗前后心功能相关参数的比较

治疗后,两组 LVESD、LVEDD、LADD 均较治疗前显著降低,LVEF 较治疗前显著升高,且观察组 LVESD、LVEDD、

表 1 两组临床治疗效果的比较[例(%)]

Table 1 Comparison of the clinical therapeutic effect between two groups[n(%)]

Groups	Case	Excellent	Valid	Invalidity	Total effective rate
Control group	30	9(30.00)	12(40.00)	9(30.00)	21(70.00)
Observation group	30	18(60.00)	10(33.33)	2(6.67)	28(93.33)
$\chi^2$					5.455
$P$					0.020

LADD 均明显低于对照组( $P < 0.05$ ), 而 LVEF 显著高于对照组 ( $P < 0.05$ ), 见表 2。

表 2 两组患者治疗前后心功能相关参数的比较( $\bar{x} \pm s$ )

Table 2 Comparison of the cardiac function parameters between two groups before and after treatment( $\bar{x} \pm s$ )

Index	Control group(n=30)		Observation group (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
LVEDD(mm)	43.86± 11.06	37.59± 9.07*	42.78± 10.57	32.09± 7.55**
LVEDD(mm)	52.36± 15.88	44.98± 10.02*	53.07± 16.12	40.01± 8.17**
LADD(mm)	42.36± 10.25	35.87± 8.62*	42.94± 11.03	30.04± 7.27**
LVEF(%)	34.25± 8.13	41.06± 9.64*	34.89± 8.64	49.31± 13.27**

注:与治疗前相比,\* $P < 0.05$ ;与对照组相比,\*\* $P < 0.05$ 。

Note: Compared with before treatment, \* $P < 0.05$ ; Compared with the control group, \*\* $P < 0.05$ .

2.3 两组治疗前后血清 cTnT、BNP、CRP 及 D-D 水平的比较 疗前显著降低, 且观察组以上指标均显著低于对照组 ( $P < 0.05$ ), 见表 3。

表 3 两组治疗前后血清 cTnT、BNP、CRP 及 D-D 水平的比较( $\bar{x} \pm s$ )

Table 3 Comparison the levels of serum cTnT, BNP, CRP and D-D between two groups before and after treatment( $\bar{x} \pm s$ )

Index	Control group(n=30)		Observation group (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
cTnT(ng/mL)	8.36± 2.04	1.87± 0.51*	8.67± 2.13	0.26± 0.07**
BNP(ng/L)	185.67± 28.54	65.38± 15.64*	186.37± 26.12	29.72± 8.25**
CRP(mg/L)	19.26± 5.11	8.32± 2.16*	18.92± 5.03	4.41± 1.34**
D-D(ng/mL)	745.28± 102.37	135.64± 20.47*	749.36± 103.56	62.38± 14.27**

注:与治疗前相比,\* $P < 0.05$ ;与对照组相比,\*\* $P < 0.05$ 。

Note: Compared with before treatment, \* $P < 0.05$ ; Compared with the control group, \*\* $P < 0.05$ .

### 2.4 两组患者出血事件发生率的比较

两组患者治疗期间均未出现严重的致死性出血事件, 观察组发生牙龈出血 1 例, 皮下出血 1 例, 出血事件发生率为 6.67%; 对照组发生牙龈出血 4 例, 皮下出血 5 例, 出血事件发生率为 30.00%。观察组出血事件发生率显著低于对照组( $P < 0.05$ )。

## 3 讨论

ACS 是心内科常见的急危重症, 其发病机制主要为冠状动脉斑块不稳定, 破裂后导致血管堵塞或狭窄, 从而引起心肌缺血缺氧, 导致心血管急性事件的发生<sup>[16-18]</sup>。有研究显示<sup>[19]</sup>ACS 发病主要与吸烟、高龄、高血压、高血脂、高血糖等有关。由于该病容易并发急性心肌梗死或猝死, 必须及早进行有效的治疗。血小板激活在 ACS 发病过程中具有重要的作用, 所以抗血小板药物的治疗具有极其重要的地位, 常与 PCI 术联合应用以改善患者的预后<sup>[20,21]</sup>。本研究将新型抗血小板药物替格瑞洛应用于老年 ACS 患者 PCI 术后, 观察其临床效果、对心功能的影响及出血事件的发生情况, 以为临床用药提供依据。

替格瑞洛具有一定的抗炎作用, 可抑制炎症细胞 P 选择素和 CD40 配体的表达, 激活内皮一氧化氮合成酶, 增加一氧化氮水平, 从而起到抗炎作用。另外, 替格瑞洛可促进腺苷的释放并抑制腺苷的摄取, 增加循环中腺苷的浓度, 腺苷通过与受体

结合促进一氧化氮介导的冠状动脉扩张, 间接改善内皮功能, 降低对心肌的损伤作用<sup>[28]</sup>。cTnT 是一种心肌收缩调节蛋白, 灵敏度和特异性均较高。当心肌发生缺血坏死时, cTnT 大量释放入血, 其水平可反映心肌损伤的程度, 是一种心肌损伤标志物<sup>[22,23]</sup>。BNP 可预测冠心病患者的病情严重程度和预后, 在 ACS 患者血清中的水平明显高于健康人群<sup>[24,25]</sup>。CRP 是一种急性时相蛋白, 临床常用的炎性标志物, 具有免疫调节作用, 可激发巨噬细胞的吞噬作用并降解细菌和异物<sup>[26]</sup>。D-D 可反映机体纤溶酶和凝血酶的活性, 监测心肌受损的程度<sup>[27]</sup>。本研究结果显示两组患者治疗后血清 cTnT、BNP、CRP 及 D-D 水平均显著降低, 且观察组显著低于对照组, 表明替格瑞洛联合阿司匹林可显著降低老年 ACS 患者的炎性反应, 降低心肌受损程度。本研究结果显示观察组治疗的总有效率显著高于对照组, 心功能相关指标显著优于对照组, 说明替格瑞洛联合阿司匹林可显著改善患者的心功能, 效果显著, 这可能与替格瑞洛联合阿司匹林可显著改善患者的 cTnT、BNP、CRP 及 D-D 水平有关。另外, 替格瑞洛本身具有活性, 口服后可直接与血小板的 P2Y<sub>12</sub> 受体结合, 不需要代谢活化, 并可快速代谢, 且代谢产物也具有活性, 具有快速强效的特点<sup>[29]</sup>。此外, 该药在停药后血小板的功能可恢复, 具有可逆性, 可保证患者的有效性和安全性<sup>[30]</sup>。本研究中, 替格瑞洛联合阿司匹林治疗的出血事件发生率较氯吡格雷联合阿司匹林更低, 提示其安全性更高。

综上所述,与阿司匹林和氯吡格雷相比,替格瑞洛联合阿司匹林可更有效显著改善老年急性冠状动脉综合征患者的心功能,且出血事件的发生率更低,可能与其显著降低血清 cTnT、BNP、CRP 及 D-D 水平有关。

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