

# 房颤合并冠心病患者经皮冠状动脉介入治疗 术后不同抗栓方案的比较

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**摘要:**目的 关于房颤(atrial fibrillation, AF)合并冠心病经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)术后患者不同抗栓方案的比较。方法 收集2015年1月—2016年6月间在滁州市第一人民医院住院治疗的90例房颤合并冠心病PCI术后患者,依据患者出院后使用的不同抗栓方案分为3组,即三联抗栓组(TT组,30例)、华法林联合氯吡格雷组(WS组,30例)、双抗组(DT组,30例)。3组其他辅助用药基本相同。记录随访12个月的临床终点事件并进行统计分析。结果 患者总体卒中风险较高(CHA2DS2-VASc评分 $\geq 2$ 分占58%),出血风险稍低(HAS-BLED $\geq 3$ 分占49%),3组总体差异均无统计学意义( $P > 0.05$ )。三联抗栓治疗组的MACCE发生率最低(6.7%),且3组差异有统计学意义( $\chi^2 = 6.193, P = 0.045$ )。采用Bonferroni法进行两两比较,结果显示,TT组和DT组有差异( $\chi^2 = 5.454, P = 0.021$ ),其余两组之间无统计学差异( $P > 0.05$ )。3组间TIMI主要出血发生率无差异( $\chi^2 = 0.000, P = 1.000$ ),三联抗栓治疗组TIMI次要出血发生率较高(13.3%),但3组差异无统计学意义( $\chi^2 = 1.098, P = 0.577$ )。结论 对于房颤合并冠心病PCI术后患者,从缺血性卒中和MACCE率来看,TT组要优于DT组,WS组与DT组和TT组之间无差异。

**关键词:**心房颤动;冠状动脉疾病;经皮冠状动脉成形术;抗栓治疗

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## Comparison of different antithrombotic therapies in patients with atrial fibrillation coronary artery disease after percutaneous coronary intervention

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**Abstract: Objective** Comparison of different strategies in patients with atrial fibrillation (AF) complicated coronary heart disease (CHD) undergoing percutaneous coronary intervention (PCI). **Methods** A total of 90 AF + CAD patients undergoing PCI were divided into trigeminy antithrombotic therapy group (TT group,  $n = 30$ ), bigeminy antithrombotic therapy group [DT group,  $n = 30$ ] and warfarin and clopidogrel group (WS group,  $n = 30$ ) based on the antithrombotic therapies after discharge; Other secondary preventions were the same in these groups. These patients were followed up around 12 months for clinical outcome events the data of which were recorded and analyzed. **Results** The overall patients had higher risk of stroke (CHA2DS2-VASc score  $\geq 2$ , 58%) and a slightly lower risk of bleeding (HAS-BLED score  $\geq 3$ , 49%), but there was no significant statistical difference ( $P > 0.05$ ). Patients with triple antithrombotic therapy had a significant reduction in stroke and major adverse cardiac and cerebral events (MACCE, 6.7%,  $\chi^2 = 6.193, P = 0.045$ ). Bonferroni pairwise comparison indicated that TT and DT groups showed statistical significance ( $\chi^2 = 5.454, P = 0.021$ ) while the other two groups had no significant difference ( $P > 0.05$ ). The results showed that there was a difference between TT group and DT group ( $\chi^2 = 5.454, P = 0.021$ ) by Bonferroni method, but there was no statistical difference between the other two groups ( $P > 0.05$ ). The incidences of major bleeding among three groups had no statistical significance ( $\chi^2 = 0.000, P = 1.000$ ). The TT group had a high rate of secondary bleeding (13.3%) but the three groups had no significant difference ( $\chi^2 = 1.098, P = 0.577$ ). **Conclusion** For patients with atrial fibrillation complicated with coronary heart disease after PCI, the rate of ischemic stroke and MACCE in TT group was better than that in other group, and there was no difference between WS group and DT group.

**Key words:** Atrial fibrillation; Coronary artery disease; Percutaneous coronary intervention; Antithrombotic therapy

房颤(atrial fibrillation, AF)为临床工作中一种常见心律失常,其发病率随年龄增长而逐渐增加<sup>[1-3]</sup>。同时因其与冠心病有相似的危险因素,所以临床上2种

疾病常常密不可分<sup>[4]</sup>。其中阿司匹林联合氯吡格雷的双重抗血小板治疗(DAPT)是经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)术后预防支架内血栓的基石<sup>[5-6]</sup>,而抗凝剂(如华法林)在预防房颤相关的体循环栓塞方面亦不可忽略<sup>[7]</sup>。房颤合并冠心病

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病患者 PCI 术后常需同时接受抗凝剂及抗血小板聚集药物,以预防动静脉血管及支架内血栓形成,因两类药物药理机制不同而无法替换,但两类药物联用又增加了出血的风险,所以如何平衡栓塞与出血风险是临床工作中的一大难点。本研究通过收集我院 90 例房颤合并冠心病 PCI 术后患者的临床资料进行整理,对比分析不同治疗方案的安全性和有效性。

## 1 资料与方法

1.1 临床资料 选取 2015 年 1 月—2016 年 6 月间在滁州市第一人民医院住院治疗,医院临床资料相对完整的房颤合并冠心病 PCI 术后患者。依据患者出院后不同的抗栓治疗方案分为 3 组:三联抗栓组(TT 组,30 例)采用华法林、阿司匹林联合氯吡格雷,华法林联合氯吡格雷组(WS 组,30 例)采用华法林、氯吡格雷;双抗组(DT 组,30 例)采用阿司匹林和氯吡格雷。其他治疗措施基本相同。入选标准:①非瓣膜性心房颤动;②冠心病;③住院期间行 PCI 术。排除标准:①有出血、对抗栓药物有禁忌证者;②患有严重肝肾疾病者;③左室射血分数 < 30% 者。

1.2 治疗方法 每组患者入院后均进行常规检查。抗栓药物分别为阿司匹林肠溶片 100 mg/d(拜耳医药保健有限公司,0.1 g × 30 片/盒),硫酸氢氯吡格雷片(原研)75 mg/d(杭州赛诺菲安万特制药有限公司,75 mg × 7 片/盒),华法林钠片(上海上药信谊药厂有限公司,2.5 mg × 60 片/盒);其中华法林一般初始剂量为 2.5 mg/d,根据国际标准化比值(INR)调整,初始为每周检测一次,若 INR 稳定在 2.0 ~ 2.5 之间,则逐渐调整为每月一次。患者一旦出现栓塞及出血等相关副反

应时,需要及时就诊并进行相应的调整。

1.3 观察指标 主要通过门诊复查及电话咨询等方式随访。当每组 INR 稳定在 2.0 ~ 2.5 之间则表示治疗方案稳定,此后每 3 个月随访 1 次,总随访期为 12 个月。主要不良心脑血管事件(MACCE)为初级终点,主要为支架内血栓、缺血性脑卒中等。安全性终点则为次级终点,采用 TIMI 出血标准分类,其中主要出血指任何出血造成血红蛋白下降 > 5 g/dl 伴有明显临床症状,而血红蛋白下降在 3 ~ 5 g/dl 间并出现明显临床症状则为次要出血。同时分别采用 CHA2DS2-VASc 评分及 HAS-BLED 评分对每组患者的栓塞和出血风险进行评估<sup>[8]</sup>。其中 CHA2DS2-VASc 评分得分越高则说明患者的栓塞几率越大。而 HAS-BLED 评分<sup>[9]</sup>总分超过 3 分则为出血事件的高危人群。

1.4 统计学方法 采用 SPSS 19.0 统计软件进行统计处理,计量资料以  $\bar{x} \pm s$  表示,多组间比较采用单因素方差分析;计数资料以百分数(%)表示,比较使用  $\chi^2$  检验或 Fisher's 确切概率法。 $P < 0.05$  为差异有统计学意义。

## 2 结果

2.1 3 组基线资料比较 3 组患者临床基线特征见表 1,其中男性 59 例,占 65.6% (59/90),平均年龄(68.39 ± 9.71)岁。通过对患者基线临床资料进行比较发现,3 组间基线数据差异无统计学意义( $P > 0.05$ )。其中,58% (52/90) 的患者 CHA2DS2-VASc 评分 ≥ 2 分,49% (44/90) 的患者 HAS-BLED 评分 ≥ 3 分,表明入选患者总体卒中风险较高,出血风险稍低,但 3 组总体差异无统计学意义( $P > 0.05$ )。

表 1 3 组房颤合并冠心病 PCI 术后患者临床基线资料比较[例(%)]

组别	例数	年龄 ( $\bar{x} \pm s$ , 岁)	男性	Hb ( $\bar{x} \pm s$ , g/L)	血小板计数 ( $\times 10^9$ )	Cr ( $\bar{x} \pm s$ , $\mu\text{mol/L}$ )	ALT ( $\bar{x} \pm s$ , IU/L)	AST ( $\bar{x} \pm s$ , IU/L)	LVEF ( $\bar{x} \pm s$ , %)	支架总数 ( $\bar{x} \pm s$ , 支)
TT 组	30	67.90 ± 9.76	21(70.0)	136.83 ± 12.29	189.83 ± 58.56	86.30 ± 24.68	18.27 ± 8.74	22.17 ± 7.21	56.50 ± 3.88	1.80 ± 0.66
WS 组	30	68.10 ± 9.68	18(60.0)	130.50 ± 15.68	186.37 ± 63.02	86.93 ± 16.11	23.43 ± 9.23	23.37 ± 7.90	56.77 ± 3.01	1.93 ± 0.64
DT 组	30	69.17 ± 9.98	20(66.7)	133.00 ± 17.65	157.50 ± 43.71	88.77 ± 23.02	23.27 ± 9.27	23.90 ± 5.20	55.63 ± 3.19	2.10 ± 0.61
统计量		0.145 <sup>a</sup>	0.689 <sup>b</sup>	1.293 <sup>a</sup>	3.046 <sup>a</sup>	0.106 <sup>a</sup>	2.327 <sup>a</sup>	0.500 <sup>a</sup>	0.922 <sup>a</sup>	0.195 <sup>a</sup>
P 值		0.866	0.709	0.280	0.053	0.900	0.104	0.608	0.076	0.117

  

组别	例数	CHA2DS2-VASc ≥ 2 分	HAS-BLED ≥ 3 分	阵发性房颤	吸烟	心衰	PPI	高血压	糖尿病	脑梗死
TT 组	30	20(66.7)	11(36.7)	9(30.0)	16(53.3)	18(60.0)	17(56.7)	11(36.7)	10(33.3)	7(23.3)
WS 组	30	18(60.0)	15(50.0)	9(30.0)	17(56.7)	17(56.7)	10(33.3)	11(36.7)	10(33.3)	8(26.7)
DT 组	30	14(46.7)	18(60.0)	16(53.3)	20(66.7)	18(60.0)	10(33.3)	14(46.7)	5(16.7)	2(6.7)
统计量		2.551 <sup>b</sup>	3.291 <sup>b</sup>	4.632 <sup>b</sup>	1.193 <sup>b</sup>	0.092 <sup>b</sup>	4.498 <sup>b</sup>	0.833 <sup>b</sup>	2.769 <sup>b</sup>	4.496 <sup>b</sup>
P 值		0.279	0.193	0.099	0.551	0.955	0.106	0.659	0.250	0.106

注: Hb 为血红蛋白; Cr 为肌酐; ALT 为丙氨酸氨基转移酶; AST 为天门冬氨酸氨基转移酶; LVEF 为左心室射血分数; PPI 为质子泵抑制剂。<sup>a</sup> 为  $F$  值, <sup>b</sup> 为  $\chi^2$  值。

2.2 随访终点事件情况 3 组患者的随访终点事件发生率见下表。三联抗栓治疗组的 MACCE 发生率最低(6.7%), 且 3 组差异有统计学意义( $\chi^2 = 6.193$ ,  $P = 0.045$ )。采用 Bonferroni 法进行两两比较, 结果显

示, TT 组和 DT 组差异有统计学意义( $\chi^2 = 5.454$ ,  $P = 0.021$ ), 其余 2 组之间差异无统计学意义( $P > 0.05$ )。3 组间 TIMI 主要出血发生率差异无统计学意义( $\chi^2 = 0.000$ ,  $P = 1.000$ ), 三联抗栓治疗组 TIMI 次要出血发

生率较高(13.3%),但3组差异无统计学意义( $\chi^2 = 1.098, P = 0.577$ ),见表2。

表2 3组房颤合并冠心病PCI术后患者随访12月临床终点事件[例(%)]

组别	例数	初级终点				次级终点		
		MI	TVR	缺血性卒中	MACCE	主要出血	次要出血	总出血事件
TT组	30	1(3.3)	1(3.3)	0(0.0)	2(6.7)	1(3.3)	4(13.3)	5(16.7)
WS组	30	1(3.3)	2(6.7)	1(3.3)	4(13.3)	1(3.3)	2(6.7)	3(10.0)
DT组	30	2(6.7)	3(10.0)	4(13.3)	9(30.0)	1(3.3)	2(6.7)	3(10.0)
$\chi^2$ 值		0.494	1.118	6.291	6.193	0.000	1.098	0.792
P值		0.781	0.572	0.043	0.045	1.000	0.577	0.672

### 3 讨论

2016 ESC/EACTS 首次联合发布房颤指南<sup>[10]</sup>,对冠心病合并房颤患者的抗栓策略与2014 EHRA/EAPCI/ACCA/HRS/APHS<sup>[11]</sup>意见基本一致,推荐抗凝方案包括:房颤合并冠心病择期行PCI术者,建议三联治疗1个月;房颤合并急性冠脉综合征(ACS)PCI术后者,则建议使用1~6个月的三联治疗。对于卒中风险为中到高危伴有出血风险为低到中危的患者,推荐相对积极的抗栓治疗;而高出血风险患者,则更倾向于口服抗凝剂联合氯吡格雷抗栓治疗方案,从而减少出血风险以获得更大的临床获益。虽然目前指南以及一些研究均对房颤合并冠心病的患者提出了治疗建议,但此类循证多来源于白种人,对于我国人群该如何抉择抗栓方案仍缺乏大量临床研究支持。因此本文就我院部分数据进行了回顾性分析,希望能提供一些有价值的信息。

通过对入选患者的基线数据进行分析发现,58%的患者CHA<sub>2</sub>DS<sub>2</sub>-VASc评分 $\geq 2$ 分,49%的患者HAS-BLED评分 $\geq 3$ 分,表明入选患者总体的卒中风险较高,出血风险稍低,3组总体差异无统计学意义( $P > 0.05$ )。三联抗栓治疗组的MACCE发生率最低(6.7%),且3组差异有统计学意义( $P = 0.044$ ),采用Bonferroni法进行两两比较,结果显示,TT组和DT组有差异( $P = 0.021$ ),其余两组之间无统计学差异( $P > 0.05$ )。3组间TIMI主要出血发生率无差异( $P = 1.000$ ),三联抗栓治疗组TIMI次要出血发生率较高(13.3%),但3组差异无统计学意义( $P = 0.722$ )。

国外一项WOEST研究<sup>[12]</sup>显示,三联抗栓法并未减少缺血事件,反而增加了出血,但该试验初级终点为出血事件,未能完全解释缺血事件的结果。同时Liu J等<sup>[13]</sup>的Meta分析显示,三联抗栓治疗更能减少栓塞事件,但也增加了出血风险。以上结果本研究数据统计相类似,但本研究纳入样本数量较少且随访时间短。此外,一些新型口服抗凝药物和抗血小板药物也为此类特殊人群带来了新的希望。其中在RELY研究中<sup>[14]</sup>,达比加群酯的抗凝地位得到了肯定,但新型抗血小板药物(普拉格雷)在三联抗栓治疗的临床试验中表明大出血风险显著高于氯吡格雷<sup>[15]</sup>,故对于此类

药物的使用,仍需大量的临床试验佐证。

综上所述,三联抗栓在降低栓塞事件的同时,也显著增加了出血风险。故而在临床工作中通过风险评估,兼顾栓塞和出血风险,实行个体化治疗方案。在出血与栓塞风险之间找到一个适合点,仍需进一步大样本量的临床试验来确定。

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度;③激活神经内啡肽系统,释放大量内源性阿片样物质,通过阿片样物质发挥镇痛和抗炎作用<sup>[20]</sup>。舒芬太尼与氯诺昔康联合应用,通过不同的镇痛机制,提高镇痛质量的同时,能够有效地减少阿片类药物的用量和副作用。

综上所述,手术结束前30 min 静脉注射舒芬太尼0.1 μg/kg + 鲁诺昔康8 mg 可减少七氟醚麻醉下鼻窦镜手术患者术后躁动的发生,且不良反应较少。

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