doi: 10.13241/j.cnki.pmb.2020.20.007

·临床研究·

替格瑞洛对行 PCI 术后患者心肌酶影响及一年随访事件相关性分析 *

郑耐心 杨国建 李 乐 张 倩 唐国栋△

（北京医院 国家老年医学中心 中国医学科学院老年医学研究院 北京 100730）

摘要 目的：研究替格瑞洛对行 PCI 术后患者心肌酶影响及一年随访事件相关性分析。**方法**：选取 2019 年 5 月至 2019 年 12 月的 133 例急性心肌梗死患者。按照随机数表法分为观察组(n=68)和对照组(n=65)，两组均采用 PCI 术治疗，术后对照组采用氯吡格雷治疗，观察组采用替格瑞洛治疗。对比两组治疗效果，心肌血流灌注指标，心肌酶变化，不良反应发生率。**结果**：治疗后，观察组总有效率显著高于对照组[95.58%(65/68)vs75.38%(49/65)]($P<0.05$)；TIMI3 级、TMPG3 级及无复流 / 满血流均显著低于对照组[17.64%(12/68)vs40.00%(26/65)，26.47%(18/68)vs46.15%(30/65)，7.35%(5/68)vs27.69%(18/65)]($P<0.05$)；LDH、CK、CK-MB 均显著低于对照组[(207.38± 21.90)U/L vs(253.75± 26.37)U/L，(166.38± 19.32)U/L vs(389.75± 52.03)U/L，(121.58± 15.86)U/L vs(162.60± 18.75)U/L]($P<0.05$)；一年随访事件发生率显著低于对照组[11.76%(8/68)vs36.92%(24/65)]($P<0.05$)。**结论**：替格瑞洛对可有效改善行 PCI 术后患者血流灌注，保护心肌细胞，改善心肌功能，提高治疗疗效。

关键词：替格瑞洛；PCI 术；心肌酶；MACE 发生率

中图分类号：R541.4 **文献标识码**：A **文章编号**：1673-6273(2020)20-3836-04

Effect of Ticagrelor on Myocardial Enzymes in Patients after PCI and Correlation Analysis of One-year Follow-up Events*

ZHENG Nai-xin, YANG Guo-jian, LI Le, ZHANG Qian, TANG Guo-dong△

(Beijing Hospital, National Center for Geriatrics, Academy of Geriatrics, Chinese Academy of Medical Sciences, Beijing, 100730, China)

ABSTRACT Objective: To study the effect of ticagrelor on myocardial enzymes in patients after PCI and correlation analysis of one-year follow-up events. **Methods:** 133 acute myocardial infarction who received therapy from May 2018 to December 2019 in our hospital were selected as research objects. According to random number table, those patients were divided into the observation group (n=68) and the control group (n=65). Both groups were treated with PCI. The control group was treated with clopidogrel. The observation group was treated with ticagrelor. The therapeutic effect, myocardial perfusion index, myocardial enzyme and Incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of control group[95.58%(65/68) vs 75.38%(49/65)] ($P<0.05$). TIMI 3, tmpg3 and no reflow / full flow were significantly lower than those in the control group [17.64%(12/68) vs 40.00%(26/65), 26.47%(18/68) vs 46.15%(30/65), 7.35%(5/68) vs 27.69%(18/65)]($P<0.05$). LDH, CK, CK-MB were significantly lower than the control group [(207.38± 21.90) U/L vs (253.75± 26.37)U/L, (166.38± 19.32) U/L vs (389.75± 52.03) U/L, (121.58± 15.86)U/L vs (162.60± 18.75) U/L] ($P<0.05$). Incidence of one-year follow-up events were significantly lower than those in the control group [11.76%(8/68)vs36.92%(24/65)]($P<0.05$). **Conclusion:** Ticagrelor can effectively improve the blood perfusion of patients after PCI, protect myocardial cells, improve myocardial function and improve the therapeutic effect.

Key words: Ticagrelor; PCI; Myocardial enzymes; MCP-1

Chinese Library Classification(CLC): R541.4 Document code: A

Article ID: 1673-6273(2020)20-3836-04

前言

急性心肌梗死是冠状动脉急性、持续性缺血缺氧所引起的心肌坏死，是临床上常见的心血管，发病率和死亡率均较高[1,2]。近年来发现[3]，该病的发生率越来越多，且呈年轻化的趋势发展。以往临床发现[4]，急性心肌梗死患者容易出现缺血而导致心肌细胞凋亡坏死，给患者的生命健康及生活质量带来了严重的威胁。目前临床上多采用经皮冠脉介入(PCI)术治疗急性心肌梗死，具有一定的治疗疗效，但冠状动脉无复流或慢血流在 PCI 术中的发生率较高，此外，PCI 术还可导致心肌标志物升高，促进炎症反应，诱发术后主要心脏不良事件(MACE)发生，不利于患者预后[5-8]。为确保 PCI 术治疗的综合效率，需要采用合理

* 基金项目：北京市自然科学基金项目(7171012)

作者简介：郑耐心(1980-)，男，本科，主治医师，研究方向：冠心病介入治疗，电话：13581814069

△ 通讯作者：唐国栋(1979-)，男，硕士，副主任医师，研究方向：冠心病介入治疗，E-mail: okedfl@163.com，电话：13581784871

（收稿日期：2020-05-06 接受日期：2020-05-30）

的药物介入治疗。替格瑞洛是新型的抗血小板聚集药物,具有起效快、作用持久的特点,可降低血栓性心血管事件的发生率。本研究旨在探讨替格瑞洛对行 PCI 术后患者心肌酶影响及一年随访事件相关性分析。

1 资料与方法

1.1 一般资料

选取 2019 年 5 月至 2019 年 12 月 133 例急性心肌梗死患者,均符合急性心肌梗死诊断标准,本研究经伦理委员会批准。纳入标准[9]:胸痛持续时间 >30 min;具有急性心肌梗死典型临床表现;存在血管病变(单支或多支);两个相邻或以上导联存在 ST 段抬高或压低;配合研究者;排除标准:患有其他严重疾病;心肝肾严重异常者;患有凝血功能障碍;对本次治疗药物过敏或不耐受者;药物治疗前采用抗血栓药物治疗者;按照简单随机数表法分为观察组(n=68)和对照组(n=65),观察组男 36 例,女 32 例,年龄 45～75 岁,平均(61.90± 2.68)岁,平均病史(6.87± 1.21)年,平均植入支架数(1.72± 0.56)个,平均病变血管数(1.60± 0.89)支,合并疾病:高血脂 21 例,高血压 32 例,糖尿病 15 例;对照组男 34 例,女 31 例,年龄 45～76 岁,平均(62.07± 2.65)岁,平均病史(6.90± 1.23)年,平均植入支架数(1.75± 0.58)个,平均病变血管数(1.65± 0.91)支,合并疾病:高血脂 19 例,高血压 29 例,糖尿病 17 例。两组一般资料均无显著差异(P>0.05),见表 1。

表 1 两组一般资料对比

Table 1 Comparison of two groups of general information

Groups	n	Gender (male / female)	Age (years)	smoke(%)	Number of stents(piece)	Number of diseased vessels (branch)	Comorbidities(%)		
							Hyperlipidemia	hypertension	diabetes
Observation group	68	36/32	61.90± 2.68	12(17.64)	1.72± 0.56	1.60± 0.89	21(30.88)	32(47.05)	15(22.05)
Control group	65	34/31	62.07± 2.65	11(16.92)	1.75± 0.58	1.65± 0.91	19(29.23)	29(44.61)	17(26.15)

1.2 方法

两组均采用 PCI 术治疗,术后给予抗心肌缺血、调脂及稳定斑块治疗,对照组在此基础上,采用氯吡格雷(生产厂家:Sanofi Winthrop Industrie)治疗,每次口服 75 mg,每天 1 次。观察组采用替格瑞洛(生产厂家:AstraZeneca AB)治疗,每次 90 mg,每天 2 次。两组治疗疗程均为 1 年,

1.3 观察指标

观察两组治疗效果,心肌血流灌注指标,心肌酶变化,MACE 发生率和不良反应率。采用深圳迈瑞生物医疗电子有限公司生产的全自动生化分析仪 (Mindray 2000)检测 LDH、CK、CK-MB 水平;对两组患者随访 1 年,记录两组随访期间不良反应发生率。TIMI3 级:造影剂完全、迅速充盈远端血管并迅速清除;TMPG3 级:造影剂进入心肌及排空正常。

1.4 疗效评定标准

心电图改善 50%以上或 T 波恢复,心绞痛疼痛程度显著减轻,绞痛次数减少 50%为显著进步[10]。心电图改善 25%～50%,疼痛程度有所减轻,绞痛次数减少 25%～50%为进步;未达到以上标准为无效。

1.5 统计学分析

使用 SPSS18.0 统计软件进行统计,数据均符合正态分布,计数资料以[(例)%]表示,用 x^2 检验比较,计量资料以($\bar{x}\pm s$)表示,采用 t 检验,组内比较使用配对样本 t 检验,采用 P<0.05 为差异有统计学意义。

2 结果

2.1 两组急性心肌梗死患者治疗效果比较

观察组总有效率显著高于对照组(P<0.05),见表 2。

表 2 两组急性心肌梗死患者治疗效果比较[例(%)]

Table 2 Comparison of the treatment effect between two groups of patients with acute myocardial infarction[n(%)]

Groups	n	Remarkable progress	Progress	Invalid	Total effective rate
Observation group	68	39(57.35)	26(38.23)	3(4.41)	65(95.58)
Control group	65	34(52.30)	15(23.07)	16(24.61)	49(75.38)

2.2 两组治疗后心肌血流灌注相关指标比较

观察组 TIMI3 级、TMPG3 级及无复流 / 满血流均显著低于对照组(P<0.05),见表 3。

2.3 两组心肌酶相关指标治疗前后的变化

两组治疗前 LDH、CK、CK-MB 均无显著差异(P>0.05),治疗后,两组 LDH、CK、CK-MB 均较治疗前显著降低(P<0.05),观察组更低(P<0.05),见表 4。

2.4 两组一年随访事件对比

观察组一年随访事件显著低于对照组(P<0.05),见表 5。

3 讨论

经皮冠脉介入(PCI)是治疗急性心肌梗死的首选方案,但术后容易发生斑块破溃、活化血小板、增加血栓发生风险[11,12]。因此,防止支架内血栓及全身动脉粥样硬化是 PCI 术后的重点

[13]。临床认为[14],抗血小板聚集可有效稳定斑块,防止斑块出血,预防患者术后不良事件发生。以往临床上多采用氯吡格雷,是一种 ADP 受体阻滞剂,在治疗急性心肌梗死上具有一定的地位[15]。但有研究发现[16-18],若长期采用氯吡格雷治疗,可严重损伤患者的血小板功能,促进血栓再形成。氯吡格雷是需要在肝脏活化,起效慢、有些患者在该药物治疗过程中会产生酶基因变异,降低抗血小板效力。且相关研究发现[19-21],氯吡格雷与血小板的二磷酸腺苷受体结合不可逆,患者停止服药后血小板需要较长的时间恢复,会延时、易发生药物间相互作用,增加出血风险。因此,无法达到满意的治疗效果。

表 3 两组治疗后心肌血流灌注相关指标比较[例(%)]

Table 3 Comparison of related indexes of myocardial blood perfusion between the two groups after treatment[n(%)]

Groups	n	TIMI3	TMPG3	No reflow / full flow
Observation group	68	12(17.64)	18(26.47)	5(7.35)
Control group	65	26(40.00)	30(46.15)	18(27.69)

表 4 两组心肌酶相关指标治疗前后的变化情况($\bar{x}\pm s$, U/L)

Table 4 Changes of myocardial enzyme related indexes before and after treatment in the two groups($\bar{x}\pm s$, U/L)

Groups	n	LDH		CK		CK-MB	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	68	315.02± 38.76	207.38± 21.90	1409.27± 386.21	166.38± 19.32	292.75± 30.82	121.58± 15.86
Control group	65	315.86± 38.90	253.75± 26.37	1410.02± 387.01	389.75± 52.03	293.01± 29.90	162.60± 18.75

表 5 两组一年随访事件对比[例(%)]

Table 5 Comparison of one-year follow-up events between the two groups [n(%)]

Groups	n	MACE	Atypical angina pectoris	syncope	Heart failure	Chest pain	Acute thrombosis
Observation group	68	2(2.94)	1(1.47)	1(1.47)	2(2.94)	1(1.47)	1(1.47)
Control group	65	8(12.30)	3(4.61)	3(4.61)	5(7.69)	3(4.61)	2(3.07)

替格瑞洛是新的 P2Y12 受体,具有生物活性,无需经肝代谢酶的生物转化,与氯吡格雷相比,具有起效快、作用持久、疗效稳定的特点,与二磷酸腺苷受体可逆性结合,可在抑制血栓形成的同时,降低出血风险[22,23]。本研究显示,采用替格瑞洛治疗的患者 LDH、CK、CK-MB 均显著低于采用氯吡格雷治疗的患者。说明了替格瑞洛可有效降低 PCI 术后患者心肌酶水平,保护患者的心肌,具有有效的修复功能。在 Filimon S[20]等作者的研究中表明,替格瑞洛可间接产生心肌及血管保护作用,可尽早促进心肌损伤修复。与本研究结果一致。

临床研究表明[24-26],血流灌注是评价 PCI 手术是否成功的关键指标,因 PCI 术会增加冠状动脉血栓负荷,患者 PCI 术后若无复流或血流减慢,会增加 MACE 的发生率。相关研究表明[27,28],PCI 术后无复流患者的死亡率是 PCI 术后恢复血流灌注患者的 10 倍,易发生恶性心血管疾病,死亡率较高。替格瑞洛可促进血栓脱落,减少血栓负荷,促进冠状动脉更快恢复血流[29,30]。本研究显示,采用替格瑞洛治疗的患者无复流、慢血流发生率显著低于采用氯吡格雷治疗的患者,TIMI3 级、TMPG3 级的比例现在高于采用氯吡格雷治疗的患者。说明了替格瑞洛能够有效促进 PCI 术后心肌灌注。但本研因研究例数较少,随访时间较短,其治疗有效性和安全性还需进一步采用更多的例数观察研究。

综上所述,替格瑞洛对可有效改善行 PCI 术后患者血流灌注,保护心肌细胞,改善心肌功能,提高治疗疗效。

参 考 文 献(References)

[1] Oner A, Aydnalp A, Haldun Mü derrisolu. Evaluation of hs-CRP and sLOX-1 Levels in Moderate-to-High Risk Acute Coronary Syndromes [J]. Endocr Metab Immune Disord Drug Targets, 2020, 20(1): 96-103

[2] Candelaria D, Randall S, Ladak L, et al. Health-related quality of life and exercise-based cardiac rehabilitation in contemporary acute coronary syndrome patients: a systematic review and meta-analysis [J]. Quality of Life Research, 2020, 29(3): 579-592

[3] Crimi G, Rosa R D, Mandurino-Mirizzi A, et al. De-escalating dual antiplatelet therapy in patients with acute coronary syndromes [J]. Journal of Cardiovascular Medicine, 2020, 21(4): 281-285

[4] Gimbel M E, Vos G J A, Nguyen T A, et al. Reasons for early discontinuing or switching of antiplatelet therapy in elderly patients after acute coronary syndrome [J]. Coronary Artery Disease, 2020, 31(1): 66-72

[5] A K O, A K H, B Y H, et al. Association between abdominal fat distribution and coronary plaque instability in patients with acute coronary syndrome [J]. Nutrition, Metabolism and Cardiovascular Diseases, 2020, 30(7): 1169-1178

[6] Scirica B M, Bergmark B A, Morrow D A, et al. Nonculprit Lesion Myocardial Infarction Following Percutaneous Coronary Intervention in Patients With AcuteCoronary Syndrome [J]. Journal of the American College of Cardiology, 2020, 75(10): 1095-1106

[7] A G D L, A M V, B S S, et al. Impact of body mass index on clinical

outcome among elderly patients with acute coronary syndrome treated with percutaneous coronary intervention: Insights from the ELDERLY ACS 2 trial [J]. Nutrition, Metabolism and Cardiovascular Diseases, 2020, 30(5): 730-737

[8] Alhumaid W , Paterson D I . Drug-Induced Acute Coronary Syndrome: A New Cardiovascular Concern With Immune Checkpoint Inhibitors and the Need for a Prospective Registry [J]. Canadian Journal of Cardiology, 2020, 36(4): 455-456

[9] Wang L, Jin Y. Noncoding RNAs as Biomarkers for Acute Coronary Syndrome[J]. BioMed Research International, 2020, 2020(40): 1-11

[10] Stefanie Schü pke, Tiroch K. Acute Coronary Syndromes and the Nontarget Lesion [J]. Journal of the American College of Cardiology, 2020, 75(10): 1107-1110

[11] Fernando Montenegro Sá, Saraiva F, Soares F, et al. Impact of frailty on hospital adverse outcomes in elderly admitted with acute coronary syndrome[J]. Galicia-clinica, 2020, 81(1): 4

[12] Donmez Y N, Aykan H H, Sahiner L. Acute coronary syndrome in an adolescent with aortic root replacement (Bentall)[J]. Cardiology in the Young, 2020, 30(3): 1-3

[13] Chetoui A, Benahmed H, Allouche E, et al. The predictive value of arterial stiffness for multivessel disease after acute coronary syndrome [J]. Archives of Cardiovascular Diseases Supplements, 2020, 12(1): 20

[14] Zhuravleva M V, Zyryanov S K, Paleev F N, et al. Effects of ticagrelor in patients with acute coronary syndrome on the targets of the national cardiovascular program [J]. Russian Journal of Cardiology, 2020, 25(5): 3931

[15] Berkovitch A, Iakobishvili Z, Fuchs S, et al. Peripheral Artery Disease, Abnormal Ankle-brachial Index and Prognosis After Acute Coronary Syndrome [J]. Journal of the American College of Cardiology, 2020, 75(11): 7

[16] Ravnkilde K, Skaarup K, Modin D, et al. Chalge in Global Longitudinal Strain and Risk of Heart Failure Following Acute Coronary Syndrome [J]. Journal of the American College of Cardiology, 2020, 75 (11): 1553

[17] Hartlein T, Krishnamurthy S, Panakos A, et al. Triple Threat: A Unique Case of Acute Coronary Syndrome From Triple-vessel Spontaneous Coronary Artery Dissection [J]. Journal of the American College of Cardiology, 2020, 75(11): 2783

[18] Meurin P, Tabet J Y, Defrance C, et al. Central sleep apnea syndrome prevalence is high early after an acute coronary syndrome without heart failure or left ventricular dysfunction[J]. Archives of Cardiovascular Diseases Supplements, 2020, 12(1): 195-196

[19] Kern A, Bojko K, Sienkiewicz E, et al. Non-st-elevation acute coronary syndrome due to a totally occluded coronary artery: a history of two twin brothers[J]. Wiadomoci lekarskie (Warsaw, Poland: 1960), 2020, 73(1): 201-202

[20] Filimon S, Nguyen H, Goldberg R J, et al. A Meta-analysis of Short-term Case-fatality Rate Among White and Black Women with acute Coronary Syndromes [J]. Journal of the American College of Cardiology, 2020, 75(11): 136

[21] Verdoia M, Suryapranata H, Damen S, et al. Prognostic Impact of Age with Short-term VS.12 Months Dual Antipatelet Therapy in Patients with Acute Coronary Syndrome: A Sub-analysis of The Reduce Trial [J]. Journal of the American College of Cardiology, 2020, 75 (11): 1229

[22] Ramlal R, Taklalsingh N, Ali R, et al. Acute Coronary Syndrome Among Young Adults with Modifiable Risk Factors Linked to Severe Coronary Artery Disease in Trinidad & Tobago [J]. Journal of the American College of Cardiology, 2020, 75(11): 3608

[23] Huang S W, Lo C H, Tsai C F, et al. Ruptured Sinus of Valsalva Aneurysm Presenting as Acute Coronary Syndrome with Cardiogenic Shock and aVR ST-Elevation - A Case Report [J]. Acta Cardiologica Sinica, 2020, 36(1): 76-80

[24] Pedro Gabriel Melo De Barros E Silva, Berwanger O, Nakagawa R, et al. Risk of Early Hospital Discharge After Acute Coronary Syndromes: Insights From Secure-pic Trial and Accept Registry[J]. Journal of the American College of Cardiology, 2020, 75(11): 13

[25] Hijazi Z, Alexander J H, Li Z, et al. Apixaban Versus Warfarin and Aspirin Versus Placebo According to Renal Function After Acute Coronary Syndrome or PCI in Atrial Fibrillation: Insights from the Augustus trial [J]. Journal of the American College of Cardiology, 2020, 75(11): 298

[26] Yusuke Uemura, Shinji Ishikawa, Kenji Takemoto, et al. Clinical outcomes after percutaneous coronary intervention in non-dialysis patients with acute coronary syndrome and advanced renal dysfunction [J]. Clinical and Experimental Nephrology, 2020, 24(4): 339-348

[27] Thomas F Lüscher. Frontiers of acute coronary syndromes: primary PCI time window, 15-year outcomes, bleeding and MINOCA [J]. European Heart Journal, 2020, 41(7): 805-809

[28] Elbaz M, Faccini J, Clémence Laperche, et al. Identification of a miRNA Based-Signature Associated with Acute Coronary Syndrome: Evidence from the FLORINF Study [J]. Journal of Clinical Medicine, 2020, 9(6): 1674

[29] Mattia Peyracchia, Andrea Saglietto, Carloalberto Biolè , et al. Efficacy and Safety of Clopidogrel, Prasugrel and Ticagrelor in ACS Patients Treated with PCI: A Propensity Score Analysis of the RENAMI and BleeMACS Registries [J]. American Journal of Cardiovascular Drugs, 2020, 20(3): 259-269

[30] Yan A T, Jong P, Yan R T, et al. Clinical trial--derived risk model may not generalize to real-world patients with acute coronary syndrome[J]. American Heart Journal, 2004, 148(6): 1020-1027