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尼可地尔联合冠状动脉心脏介入治疗冠心病合并肾功能不全的疗效及对 NGAL、Cys-C 的影响 *

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摘要 目的: 探讨冠心病(CHD)合并肾功能不全(RI)应用冠状动脉心脏介入治疗(PCI)联合尼可地尔的临床疗效及对胱抑素 C(Cys-C)、中性粒细胞明胶酶相关脂质运载蛋白(NGAL)影响。**方法:** 选择本院 2019 年 6 月~2021 年 6 月就诊的 86 例 CHD 合并 RI 患者,随机数字表法分为两组各 43 例。两组均实施 PCI 治疗,对照组实施常规静脉水化处理,观察组联合尼可地尔治疗。对比两组 PCI 治疗前后 24 h 肾功能指标(Cys-C、NGAL)、血清炎症因子指标(高敏 C 反应蛋白(hs-CRP)、白细胞介素 6(IL-6))、心肌损伤指标(心肌肌钙蛋白 I(cTnI)及肌酸激酶同工酶(CK-MB))、并发症发生率。**结果:** 观察组 CIN 发生率(2.33%)、MACE 率(2.33%)均明显低于对照组(16.28%、13.95%),有统计学差异($P<0.05$)。两组 PCI 治疗前 Cys-C、NGAL、hs-CRP、IL-6、cTnI、CK-MB 无统计学差异($P<0.05$)。治疗后观察组 Cys-C、NGAL、hs-CRP、IL-6 升高幅度、组 cTnI、CK-MB 明显低于对照组($P<0.05$)。**结论:** PCI 联合尼可地尔应用于 CHD 合并 RI 临床治疗效果显著,可有效改善患者肾功能,降低炎症反应、心肌损伤,预防 CIN 发生。

关键词: 尼可地尔; 冠状动脉心脏介入; 冠心病; 肾功能不全; NGAL; Cys-C

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Effect of Nicorandil Combined with Coronary Intervention on Coronary Heart Disease Combined with Renal Insufficiency and its Influence on NGAL and Cys-C*

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ABSTRACT Objective: To explore the clinical effects of coronary heart disease (CHD) combined with renal insufficiency (RI) using coronary heart intervention (PCI) combined with nicorandil and its effects on cystatin C(Cys-C) and neutrophil gelatinase-associated lipocalin (NGAL). **Methods:** A total of 86 cases of CHD combined with RI who visited our hospital from June 2019 to June 2021 were selected and randomly divided into two groups with 43 cases in each group according to random number table. Both groups were treated with PCI, while the control group was treated with conventional intravenous hydration and the observation group was treated with nicorandil. The renal function indexes (Cys-C and NGAL) at 24 h, serum inflammatory factor indexes (high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6)), myocardial injury indexes (cardiac troponin I(cTnI) and creatine kinase isoenzyme (CK-MB)) and the incidence of complications before and after PCI were compared between the two groups. **Results:** The incidence of CIN (2.33%) and MACE (2.33%) in the observation group were significantly lower than those in the control group (16.28% and 13.95%), with statistical difference ($P<0.05$). There was no statistical difference in Cys-C, NGAL, hs-CRP, IL-6, cTnI, and CK-MB between the two groups before PCI ($P<0.05$). After treatment, the increases in Cys-C, NGAL, hs-CRP, and IL-6 as well as the cTnI and CK-MB in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** PCI combined with nicorandil has significant effect in the clinical treatment of CHD combined with RI, which can effectively improve renal function, reduce inflammation, myocardial damage and prevent the occurrence of CIN.

Key words: Nicorandil; Coronary heart intervention; Coronary heart disease; Renal insufficiency; NGAL; Cys-C

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前言

冠心病(CHD)属于临床常见中老年疾病,据相关研究报道肾功能不全(RI)为CHD的高危因素,且RI与CHD预后质量存在密切关联性,因此临床CHD合并RI发病率极高,且治疗难度相对较高,积极控制疾病进展有利于改善预后质量^[1-3]。冠状动脉介入治疗(PCI)属于临床常用治疗CHD合并RI手术,可以有效改善冠脉狭窄及闭塞,恢复正常心肌供血,继而有效缓解CHD临床症状^[4,5]。但是近年来有研究显示PCI中对比造影剂的应用对患者肾功能、心功能有着严重影响,应用造影剂后对比剂肾病(CIN)发生率也越来越高,一旦CIN发生将会造成不可逆肾损伤,因此研究PCI治疗的可行性及安全性已经成为临床重要研究课题^[6-11]。尼可地尔属于ATP敏感性钾离子通道开放剂,是临床研究首个具有类硝酸酯功效的离子通道开放剂,既往常用于CHD临床治疗,可以通过开放冠脉,有效改

善冠脉微循环^[12-14]。近年来有研究显示尼可地尔应用于CHD合并RI患者中可以有效预防PCI的不良影响,如心功能、肾功能损害预防等。但是临床对其研究报道不够全面,且相关报道较少^[15-17]。基于此,本研究将对尼可地尔联合PCI应用于CHD合并RI的临床疗效及对NGAL、Cys-C影响进行分析,旨在为临床CHD合并RI患者提供更加安全有效的治疗策略。试验报道如下:

1 资料与方法

1.1 一般资料

选择本院2019年6月~2021年6月就诊的86例CHD合并RI患者,随机数字表法分为两组各43例。两组CHD合并RI患者一般资料(性别、年龄、病程、体质指数、合并症)对比均无统计学差异($P < 0.05$)。见表1。

表1 两组CHD合并RI患者一般资料对比[n(%)]

Table 1 Comparison of general data of CHD patients with RI between two groups[n(%)]

Groups	Number of cases	Gender (male/female)	Age (years)	Course of disease (years)	Body mass index (kg/m ²)	Comorbidities (hypertension/diabetes)
Observation group	43	30/13	64.78±12.34	3.17±1.05	24.37±2.15	27/24
Control group	43	29/14	64.95±12.13	3.09±1.12	24.46±2.13	25/26
χ^2/t	-	0.054	0.064	0.342	0.195	0.195
P	-	0.816	0.948	0.733	0.846	0.659

纳入标准:①符合符合《冠心病心脏康复基层合理用药指南》^[18]CHD诊断标准及《老年人慢性肾脏病诊治中国专家共识(2018)》^[19]RI临床症状及相关影像学、实验室诊断标准;②符合《中国经皮冠状动脉介入治疗指南(2016)》^[20]治疗适应症者;③患者及家属共同签署知情同意书。

排除标准:①对本研究PCI对比剂过敏或存在严重肾功能不全者;②合并心功能不全、多器官障碍、心肌梗死、炎症疾病、血流动力学不稳定等严重疾病者;③近期末服用尼可地尔治疗者。

1.2 方法

两组均实施PCI治疗,对比剂选择碘普胺370,术前12h-术后12h过程中基于持续补液治疗,对照组实施常规静脉水化处理,持续静脉滴注0.9%氯化钠注射液,速度维持在1.0 mL/(h·kg)。观察组联合尼可地尔(生产厂家:京四环科宝制药有限公司,规格:12 mg,国药准字:H20120069),持续静脉滴注尼可地尔注射液(48 g注射用尼可地尔+500 mL 0.9%氯化钠注射液),速度维持在1.0 mL/(h·kg)。

1.3 观察指标

对比两组肾功能指标:采集PCI治疗前后24h时间点肘静脉血4 mL,进行肝素抗凝及离心操作(1000 r/min, 30 Min),分离血清并放置低温冰箱中进行保存待测,采用免疫比浊法检测胱抑素C(Cys-C)(试剂盒来源上海起发实验试剂有限公司)、酶联免疫吸附(ELISA)检测中性粒细胞膜脂酶相关脂质运载蛋白(NGAL),试剂盒来源R&D Systems公司。

对比两组血清炎症因子指标:于治疗前后24h,采用免疫比浊法检测高敏C反应蛋白(hs-CRP),采用ELISA检测白细胞介素6(IL-6),试剂盒均来源于南京建成生物工程研究所

有限公司。

对比两组心肌损伤指标:于治疗前后24h,采用免疫荧光层析法及对应试剂盒检测心肌肌钙蛋白I(cTnI)及肌酸激酶同工酶(CK-MB)指标,试剂盒均来源于青岛市三凯医学科技有限公司。

对比两组并发症发生率:统计治疗过程中发生对比剂肾病(CIN)及不良心血管事件(MACE)(包括心绞痛、急性心肌梗死)等并发症发生率。参照《冠心病介入诊疗对比剂应用专家共识(2014版)》^[21]制定标准,术后3d,Scr相对增加超过基线1/4或≥44.2 mmol/L(0.5 mg/dl)。

1.4 统计学方法

将数据纳入SPSS23.0软件中分析,计量资料比较采用t检验,并以($\bar{x} \pm s$)表示肾功能指标、心肌损伤、炎症因子指标,计数资料采用 χ^2 检验,并以率(%)表示并发症发生率, ($P < 0.05$)为有统计学差异。

2 结果

2.1 对比两组CIN发生率

观察组CIN发生率(2.33%)、MACE率(2.33%)均明显低于对照组(16.28%、13.95%),有统计学差异($P < 0.05$)。见表2。

2.2 对比两组肾功能指标

两组PCI治疗前肾功能指标(Cys-C、NGAL)无统计学差异($P < 0.05$)。治疗后观察组Cys-C、NGAL明显低于对照组($P < 0.05$)。见表3,图1。

2.3 对比两组炎症因子指标

两组PCI治疗前炎症因子指标(hs-CRP、IL-6)无统计学差

异($P<0.05$)。治疗后两组均明显升高,且观察组 hs-CRP、IL-6 升高幅度明显低于对照组($P<0.05$)。见表 4,图 2。

表 2 对比两组临床疗效[n,(%)]

Table 2 Comparison of clinical effects between the two groups [n,(%)]

Groups	Number of cases	CIN	Angina pectoris	Acute myocardial infarction	MACE rate
Observation group	43	1(2.33)	0(0.00)	1(2.33)	1(2.33)
Control group	43	7(16.28)	2(4.65)	4(9.30)	6(13.95)
χ^2	-	4.962	-	-	3.888
P	-	0.026	-	-	0.049

表 3 对比两组肾功能指标($\bar{x} \pm s$)Table 3 Comparison of the functional indicators of both kidneys($\bar{x} \pm s$)

Groups	Number of cases(n)	Cys-C (mg/L)		NGAL (ngmL)	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Observation group	43	1.28 $\pm$ 0.23	1.21 $\pm$ 0.18	64.78 $\pm$ 25.32	71.45 $\pm$ 27.34
Control group	43	1.27 $\pm$ 0.32	1.59 $\pm$ 0.37	64.82 $\pm$ 25.17	85.24 $\pm$ 28.17
t	-	0.166	6.056	0.007	2.304
P	-	0.868	0.001	0.994	0.024

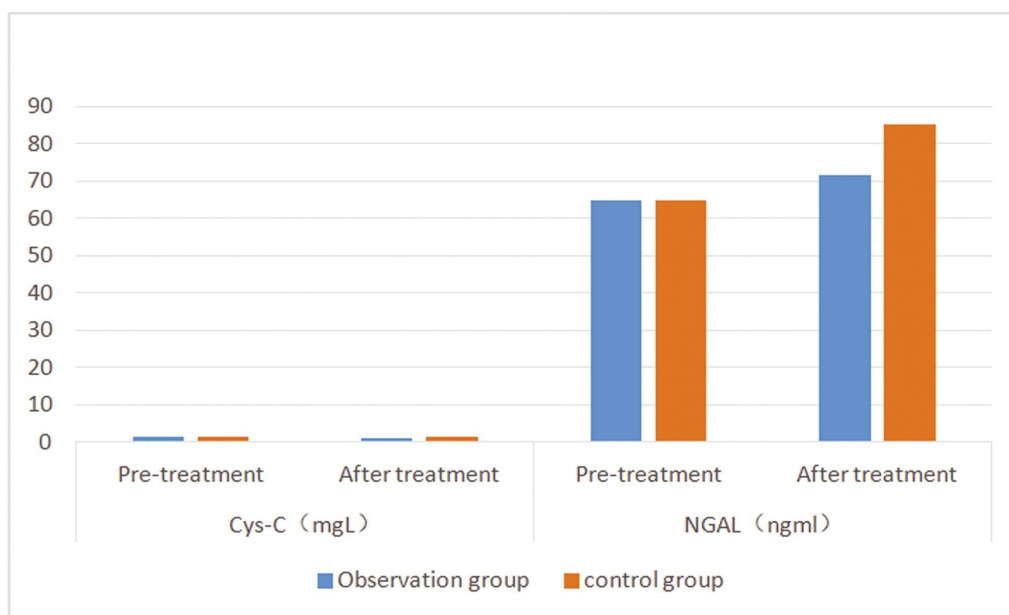


图 1 双肾功能指标的比较

Fig.1 Comparison of the functional indicators of both kidneys

表 4 对比两组炎症因子指标($\bar{x} \pm s$)Table 4 Comparison of two groups of indicators of abdominal mass($\bar{x} \pm s$)

Groups	Number of cases(n)	hs-CRP (mmol/L)		IL-6 (ng/L)	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Observation group	43	0.41 $\pm$ 0.13	1.02 $\pm$ 0.35	124.78 $\pm$ 12.65	134.27 $\pm$ 15.26
Control group	43	0.44 $\pm$ 0.12	1.45 $\pm$ 0.37	125.03 $\pm$ 12.14	151.34 $\pm$ 16.78
t	-	1.112	5.536	0.094	4.935
P	-	0.269	0.001	0.926	0.001

2.4 对比两组心肌损伤指标

两组 PCI 治疗前心肌损伤指标(cTnI、CK- MB)无统计学

差异($P<0.05$)。治疗后观察组 cTnI、CK- MB 明显低于对照组($P<0.05$)。见表 5,图 3。

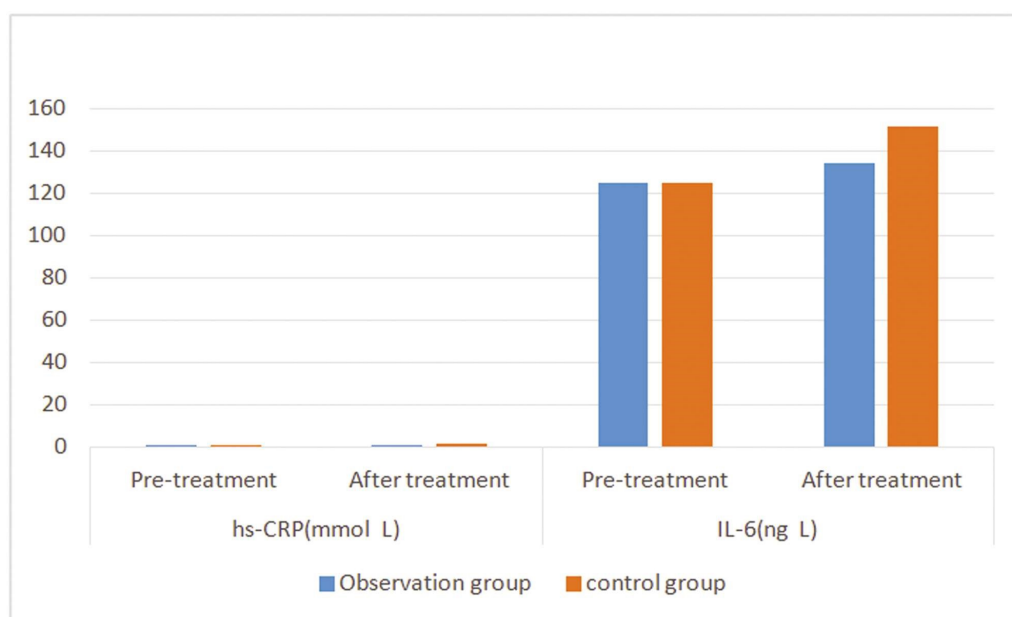


图 2 两组腹部质量指标的比较

Fig.2 Comparison of two groups of indicators of abdominal mass

表 5 对比两组心肌损伤指指标($\bar{x} \pm s$)

Table 5 Comparison of indicators of two groups of myocardial losses($\bar{x} \pm s$)

Groups	Number of cases(n)	cTnI(ng/mL)		CK- MB(U/L)	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Observation group	43	0.07± 0.03	0.14± 0.05	6.14± 0.38	14.26± 4.51
Control group	43	0.06± 0.02	0.39± 0.11	6.11± 0.43	21.32± 5.67
t	-	1.819	13.567	0.343	6.390
P	-	0.073	0.001	0.733	0.001

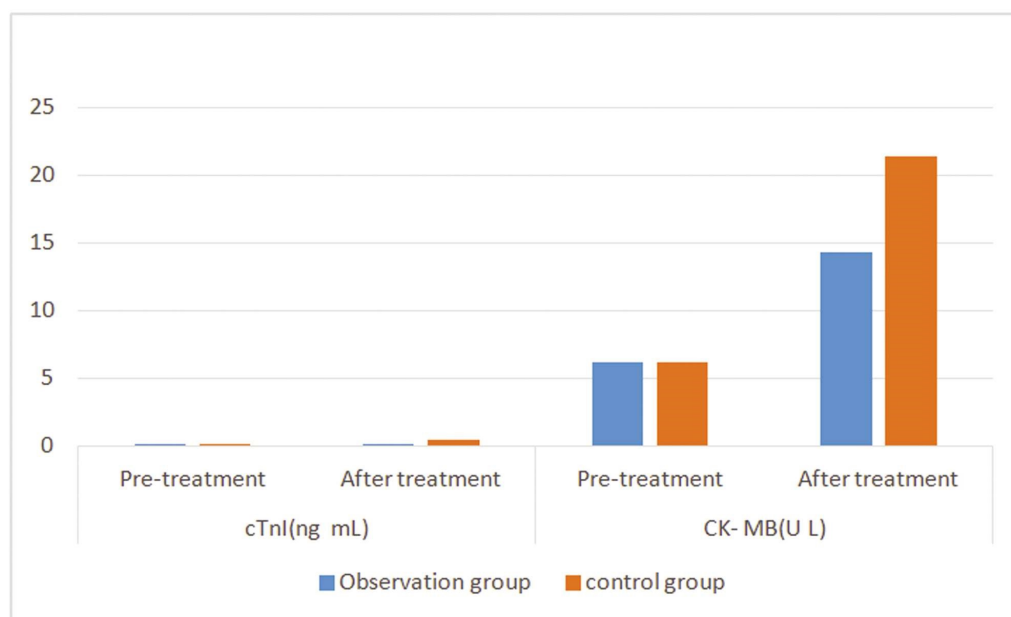


图 3 两组心肌损失指标的比较

Fig.3 Comparison of indicators of two groups of myocardial losses

3 讨论

HD 患者常常伴随着高血压、糖尿病等基础疾病,发生 RI

概率极高,而 RI 后将会促使机体持续处于氧化应激状态,诱发全身炎症反应,加重 CHD 病情。近年来随着临床对 CHD 合并 RI 研究的深入,PCI 治疗技术也在快速发展,且得到广泛应

用^[20]。但是目前诸多研究显示 PCI 在 CHD 合并 RI 中应用尚存在争议,治疗过程中应用造影剂对患者肾功能会造成一定损害,继而加重肾功能不全病情,研究显示,肾功能不全是 PCI 预后不良的重要预测因素^[21]。CIN 属于 PCI 治疗中应用碘对比剂的严重并发症,也是发生获得性急性肾损伤的主要因素,其发病机制尚未完全阐明^[22],临床认为可能与以下因素存在密切联系,其一,对比剂进入人体肾血管后导致其短暂快速扩张,肾血流量也随之上升,而血管阻力同时伴随增加以及长时间血管收缩,导致其血流量持续下降,血流动力学快速波动引起肾血管肾髓质缺血缺氧双相反应;其二,对比剂可以显著降低肾小管上皮细胞生物活性,引发机体高脂质过氧化反应,合成氧自由基,继而诱导氧化应激损伤;其三对比剂对于肾小管上皮细胞、血管内皮细胞存在直接细胞毒效应,发生空泡样改变和胞质溶酶体改变,氧化应激、缺氧等病理症状共同延长毒性作用,加剧肾功能损伤。随着临床 PCI 技术的推广,碘对比剂引起的 CIN 也逐渐得到临床关注,CHD 合并 RI 患者自身肾脏功能较弱,对对比剂清除能力不高,发生 CIN 概率极高,有必要加强诊断及预防管控。

选择诊断 CIN 的依据特异性反映肾脏结构及功能损伤是临床研究重点之一。既往主要采用 Scr 评估,仍存在一定滞后性及低敏感性应用局限,受到蛋白质摄入、药物等因素影响,且 Scr 变化滞后于肾损伤,不利于早期肾脏干预。NGAL 属于脂质运载蛋白,其作用机理主要发挥抗炎、减少氧化应激等重要生理功能,主要分布于皮质肾小管、血液、尿液中,有研究显示 NGAL 在对比剂治疗应用后敏感性较高,在术后 2 h 可以出现显著升高,4 h 可以达到峰值^[23]。Cys-C 属于胱氨酸蛋白酶抑制剂,可以敏感反映肾小球损伤进度,其影响冠心病作用机制如下:Cys-C 可以通过降低半胱氨酸蛋白酶(Caspase)等冠心病相关酶功能活性,促使细胞外基质过度降解,促使粥样斑块发生破裂,继而导致脂质沉积;抑制 Caspase 降解,提高机体氧化型脂蛋白分泌,促进血小板积聚,继而损害到机体内皮功能等等。有研究显示 Cys-C 可以评估肾损伤严重程度,有利于尽早控制 CIN 发生。因此本研究选择 NGAL、Cys-C 指标作为评估预防疗效依据^[24,25]。

既往临床针对 PCI 后发生 CIN 主要采用水化预防,通过保证肾脏血流通畅,促进对比剂排泄,稀释对比剂浓度,降低对肾小管细胞毒性等机制发挥预防功效,但是针对合并 RI 患者治疗效果不够显著,还需要对其预防药物做进一步研究^[26]。尼可地尔具有类硝酸酯、K⁺-ATP 通道开放剂双重功效,其药理作用如下:其一,尼可地尔通过促进细胞内大量流出 K⁺,并抑制钙离子流入细胞,防止其线粒体内离子超载,恢复线粒体正常功能,发挥舒张血管,提高冠脉血流量功效,模拟心肌缺血预适应,减少缺血再灌注损伤,继而保护心肌细胞,改善心功能指标^[27]。其二,尼可地尔可以通过直接作用于线粒体上离子通道,降低氧化自由基合成,减轻氧化应激反应引起的肾脏的损害;同时可以增加一氧化氮减轻肾血管收缩引发的肾脏损害^[28,29]。其三,尼可地尔可以发挥与硝酸酯类药物相似的作用,通过一氧化氮依赖的方式,直接激活血管平滑肌细胞中鸟苷酸环化酶,平滑肾血管平滑肌,扩张肾动脉,改善肾缺血再灌注损伤,发挥抗炎、抗氧化功效,继而减轻炎症病理反应^[30,31]。

本研究结果显示,治疗后观察组 Cys-C、NGAL、hs-CRP、IL-6 升高幅度、组 cTnI、CK-MB 明显低于对照组($P<0.05$)。NGAL、Cys-C、Scr 指标均可以敏感反映肾功能损伤情况及损伤程度,而联合尼可地尔可以进一步提高临床疗效,该药物可以发挥抗凝、预防血栓形成、减轻肾脏缺血再灌注损伤、增加心肌供血供氧量,减轻氧化应激反应等多重功效。观察组 CIN 发生率(2.33%)、MACE 率(2.33%)均明显低于对照组(16.28%、13.95%),有统计学差异($P<0.05$)。由此可见联合尼可地尔可以充分发挥早期肾保护功效,降低 CIN 发生率。其原因在于持续水化治疗对于造影剂有一定稀释作用,继而促进肾脏排泄,同时通过促进血管扩张及血液流量循环,减轻肾毒性,但是这种预防功效效果仍不够理想。联合尼可地尔可以进一步抑制对比剂的肾毒性,起到较好预防 CIN 效果,并通过减轻心肌损伤,降低心血管不良事件^[32]。此外由于本研究样本数量较少,且试验为单中心研究,研究存在一定局限性,还需要更多大样本、多中心对照研究给予实证支持。

综上所述,PCI 联合尼可地尔应用于 CHD 合并 RI 临床治疗效果显著,可有效改善患者肾功能,降低炎症反应、心肌损伤,预防 CIN 发生。

参考文献(References)

- [1] Núñez Julio, Lorenzo Miguel, Miñana Gema, et al. Sex differences on new-onset heart failure in patients with known or suspected coronary artery disease[J]. *European journal of preventive cardiology*, 2021, 28 (15): 1711-1719
- [2] Xia Si-liang, Zhang Xiao-bing, Yin Ke-jin. Clinical characteristics and interventional treatment in patients with coronary artery spasm and angina pectoris[J]. *Chinese Clinical Studies*, 2020, 33(8): 1058-1061
- [3] Mustafa Duran, Deniz Elcik, Mehmet T Inanc, et al. Relationship between mild renal dysfunction and coronary artery disease in young patients with stable angina pectoris [J]. *Biomark. Med.*, 2020, 14 (6): 433-440
- [4] ŁUKASZ KUŻMA, JOLANTA MAŁYSZKO, ANNA KURASZ, et al. Impact of renal function on patients with acute coronary syndromes: 15,593 patient-years study[J]. *Renal Failure*, 2020, 42(1): 881-889
- [5] Xu Xiao-jin, Zhang Qing, Wang Bing-jian, et al. Relevant factors of postoperative interventional contrast nephropathy and the early diagnosis value of urinary NGAL on contrast nephropathy in patients with coronary heart disease[J]. *The Heart Journal*, 2019, 31(1): 12-16, 21
- [6] Misawa Toru, Sugiyama Tomoyo, Kanaji Yoshihisa, et al. Effect of contrast medium versus low-molecular-weight dextran for intracoronary optical coherence tomography in renal insufficiency [J]. *The international journal of cardiovascular imaging*, 2021, 37(9): 2603-2615
- [7] Ali, Ghorbani, Saeed, et al. Prevention of Contrast-induced Nephropathy in Patients with Chronic Kidney Disease Undergoing Elective Coronary Angioplasty or Angiography with Sodium Potassium Citrate Solution, a Double Blind Randomized Clinical Trial [J]. *Iranian journal of kidney diseases*, 2019, 13(3): 182-190
- [8] Tian Guo-xiang, WuYun-tao, Yao Lu, et al. Clinical efficacy of Nicadil in older patients with coronary multiple lesions combined with angina attack and cardiac insufficiency[J]. *Chinese Journal of Evidence-Based Cardiovascular Medicine*, 2019, 11(6): 694-697
- [9] Li Xihui, Xiao Feng, Zhang Siyu. Coronary revascularization in pa-

- tients with chronic kidney disease and end-stage renal disease: a meta-analysis [J]. *International journal of clinical practice*, 2021, 75 (11): e14506
- [10] Zhang Qin-yao, Ma Shu-mei. myocardial protection of intravenous Nicorl in patients with unstable angina undergoing percutaneous coronary intervention [J]. *Practical drugs and clinical*, 2020, 23(1): 38-42
- [11] Li Qiang, Li Yan-bing, Chen Ming, et al. Efficacy of nicoxidil combined with atorvastatin on the treatment of slow coronary blood flow phenomenon and its effect on the recent prognosis [J]. *Journal of Clinical Cardiovascular Disease*, 2019, 35(8): 697-701
- [12] Guan Bing, Su Yang, Wei Xu-bin, et al. Effect of Nicadl on coronary microcirculation disorder in patients with obstructive coronary heart disease [J]. *Journal of Kunming Medical University*, 2020, 41 (2): 68-75
- [13] Zhu Yuan-yuan, He Shao-hui, Liu Mei-lin, et al. Effect of Nicoxidil on angina patients treated with percutaneous coronary intervention [J]. *Journal of Practical Cardiovascular Disease*, 2019, 27 (10): 95-99
- [14] Liu Qiang, Sun Min, Wang Shi-feng, et al. Effect of prodil combined with Niccodil on percutaneous coronary intervention in patients with unstable angina[J]. *Journal of Practical Cardiovascular Disease*, 2019, 27(6): 86-89
- [15] Zhang Peng, Zhang Xue, Yang Shi-cheng, et al. Prevention of Nicadl on contrast nephropathy for renal insufficiency in percutaneous coronary intervention [J]. *Chinese Journal of New Drugs and Clinical Medicine*, 2020, 39(6): 357-362
- [16] Ma Yu-feng, He Ling, Zhang Ke-sen, et al. Prevention of Nicodl on contrast nephropathy after coronary intervention [J]. *Chinese Medicine*, 2019, 14 (10): 1462-1466
- [17] Wang Lei, Chen Yun-dai, Tian Feng. Application and Progress of Nicadl in the Treatment of Coronary Heart Disease [J]. *Journal of Integrated Traditional Chinese and Western Medicine*, 2020, 18 (9): 1400-1402
- [18] Chinese Medical Association, Clinical Pharmacy Branch of Chinese Medical Association, *Journal of Chinese Medical Association*, et al. Guidelines for Basic Rational Use of Coronary Heart Disease Rehabilitation [J]. *Chinese Journal of General Practice*, 2021, 20 (3): 311-320
- [19] Nephrotic Group, Chinese Society of Geriatrics, National Clinical Research Center for Geriatric Diseases. Chinese Expert Consensus on the Diagnosis and Treatment of Chronic Kidney Diseases in the Elderly (2018)[J]. *Chinese Journal of Geriatrics*, 2018, 37(7): 725-731
- [20] Tzoumas Andreas, Tzani Aspasia, Doulamis IliasI, et al. TCT CON-NECT-158 Percutaneous Coronary Intervention With Drug Eluting Stents Versus Coronary Artery Bypass Grafting in Patients With Impaired Renal Function: A Systematic Review and Meta-Analysis[J]. *Journal of the American College of Cardiology*, 2020, 76 (17): B67-B68
- [21] Shafik Khoury, Gilad Margolis, Zach Rozenbaum, et al. Acute renal impairment in older adults treated with percutaneous coronary intervention for ST-segment elevation myocardial infarction [J]. *Coronary Artery Disease*, 2019, 30(8): 564-568
- [22] KAHKONEN, OUTI, SAARANEN, TERHI, KANKKUNEN, PAIVI, et al. Adherence to Treatment of Female Patients With Coronary Heart Disease After a Percutaneous Coronary Intervention [J]. *The Journal of cardiovascular nursing*, 2019, 34(5): 410-417
- [23] Yi Heng-liang, Sun Yu, Liu Jun, et al. Correlation and Clinical Significance of Serocysteine C, urinary Kidney Injury Molecular 1 and contrast nephropathy [J]. *Medical Clinical Study*, 2019, 36 (5): 917-918, 921
- [24] Kang Mei-li, Jin Peng. Study on the correlation between Serum Cys-C and HMGB1 and the occurrence and severity of Coronary Heart Disease[J]. *Journal of Integrated Traditional Chinese and Western Medicine*, 2020, 18(2): 271-274
- [25] Ao Qiang-guo. Progress in the study of endogenous biomarkers of kidney injury [J]. *Chinese Journal of Clinical Health Care*, 2020, 23 (1): 35-41
- [26] Liu Chun, Ling Ming-ying, Li Xue-hui, et al. Study on Kidney Protection of exogenous Phosphorinatin in elective coronary heart disease [J]. *Journal of Practical Cardiovascular Disease*, 2019, 27(4): 1-7
- [27] Houyong, Zhu, Xiaoqun, et al. Effects of the Antianginal Drugs Ranolazine, Nicorandil, and Ivabradine on Coronary Microvascular Function in Patients With Nonobstructive Coronary Artery Disease: A Meta-analysis of Randomized Controlled Trials[J]. *Clinical therapeutics*, 2019, 41(10): 2137-2152
- [28] Lu Ai-min, Liu Bao-bao, Chen Rong. Effect of nicorl and clopidogrel in patients with coronary heart disease and its effect on serum Lp (a) and CX3CL1[J]. *Hebei Medicine*, 2019, 41(10): 1542-1545
- [29] Lu Li-jie, Zhu Yong-xiang, Li Feng, et al. Meta-analysis of Nicadl preventive contrast nephropathy [J]. *Chinese Cardiovascular Journal*, 2021, 26(3): 277-281
- [30] Fan Yan-ming, Cai Jun-na, Zhang Bo, et al. Prophylactic effect of oral Nicodl on direct PCI contrast nephropathy in patients with acute ST-segment elevation myocardial infarction [J]. *Chinese Journal of Evidence-Based Cardiovascular Medicine*, 2019, 11(11): 1333-1336
- [31] Liu Zu-xia, Zhang Bin, Wang Wei. Effects of Nicoxidil on Vascular endothelial Function and Seroinflammatory Response in Patients with PCI Coronary Heart Disease[J]. *Journal of Cardiovascular Rehabilitation*, 2019, 28(3): 337-341
- [32] Wu Yuan-yuan, Cao Xiao-zhi, Wang Zhi-qing, et al. Effect of nicodil combined with teagrello on myocardial blood perfusion after direct percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction [J]. *Chinese Journal of Circulation*, 2019, 34(4): 343-350