

doi: 10.13241/j.cnki.pmb.2017.01.014

# 老年心肌梗死患者 PCI 术后心率变异性的变化及丹参滴丸的临床疗效研究\*

欧 更 姜明燕 郜琪臻 陈 莹 刘 妍

(中国医科大学附属第一医院 药剂科 辽宁 沈阳 110001)

**摘要 目的:**探究老年心肌梗死患者经皮冠状动脉介入治疗(PCI)术后心率变异性的变化及实施 PCI 治疗后给予丹参滴丸的临床疗效。**方法:**收集 2015 年 3 月到 2016 年 3 月来我院就诊的老年急性心肌梗死患者 56 例,根据随机数字表法分为试验组及对照组,各 28 例,对所有患者实施 PCI 术,术后对照组使用基础药物治疗,试验组使用基础药物治疗联合复方丹参滴丸。比较 PCI 治疗前后心率变异性的变化及两组患者的心功能。**结果:**PCI 术后,患者测定指标 SDNN、SDNN Index 及 SDANN 相对于术前均有升高( $P<0.05$ );频域分析指标 HF 及 LF 相对于术前均升高,LF/HF 比值降低( $P<0.05$ )。治疗结束后,两组患者 LVEF、SV 及 CI 均明显升高,LVEDD 明显降低( $P<0.05$ ),与对照组相比,试验组患者 LVEF、SV 及 CI 较高,LVEDD 较低( $P<0.05$ )。**结论:**PCI 术能够改善老年心肌梗死患者心率变异性,而复方丹参滴丸对于 PCI 术后老年心肌梗死患者心功能指标均有明显改善,临床疗效较好。

**关键词:**老年心肌梗死;经皮冠状动脉介入治疗;心率变异性;丹参滴丸

中图分类号:R542.22 文献标识码:A 文章编号:1673-6273(2017)01-59-03

## Study on the Clinical Curative Effect of Danshen Dripping Pill in the Treatment of Heart Rate Variability in Elderly Patients with Myocardial Infarction after PCI\*

OU Geng, JIANG Ming-yan, GAO Qi-zhen, CHEN Ying, LIU Yan

(Department of Pharmacy, the First Affiliated Hospital, China Medical University, Liaoning, Shenyang, 110001, China)

**ABSTRACT Objective:** To investigate the clinical curative effect of danshen dripping pill in the treatment of heart rate variability in elderly patients with myocardial infarction after PCI. **Methods:** 56 elderly patients with acute myocardial infarction in our hospital from March 2015 to March 2016 were selected and randomly divided into the control group and the experiment group with 28 cases in each group. All patients underwent PCI, the control group was treated by basic medicine and the experiment group was treated by basic drug therapy combined with compound Danshen dripping pills. The changes of heart rate variability before and after PCI treatment and clinical efficacy of two groups were compared. **Results:** The SDNN, SDNN Index and SDANN levels were higher postoperative PCI ( $P<0.05$ ). The Frequency domain analysis index HF and LF levels were higher postoperative PCI ( $P<0.05$ ), the LF/HF ratio was lower ( $P<0.05$ ). At the end of treatment, the LVEF, SV and CI levels were higher ( $P<0.05$ ), the LVEDD was lower ( $P<0.05$ ). Compared with the control group, the LVEF, SV and CI levels were higher ( $P<0.05$ ), the LVEDD was lower ( $P<0.05$ ). **Conclusion:** PCI could improve the heart rate variability in elderly patients with myocardial infarction, and compound Danshen dripping pills significantly improved cardiac function of elderly patients with myocardial infarction after PCI.

**Key words:** Senile myocardial infarction; PCI; Heart rate variability; Danshen dripping pill

**Chinese Library Classification(CLC):** R542.22 **Document code:** A

**Article ID:** 1673-6273(2017)01-59-03

### 前言

心肌梗死是由于冠状动脉狭窄导致的心肌缺血坏死,可引起心力衰竭等严重并发症<sup>[1]</sup>,目前临床上主要采用药物治疗及再灌注治疗。经皮冠状动脉介入治疗(PCI)是近几年新兴的治疗方法,属于再灌注治疗的一种,能够解除冠状动脉狭窄,改善心肌梗死症状<sup>[2]</sup>。研究显示心率变异性(HRV)可评价交感-迷走神经张力是否达到平衡状态,与循环系统功能密切相关,能够作

为评价 PCI 术后心肌梗死严重程度的无创性指标<sup>[3]</sup>。

复方丹参滴丸作为我国传统中药,具有通畅血脉的功效<sup>[4]</sup>,近年来发现其具有扩张冠状动脉、抗血小板凝集等功效,能够缓解急性心肌梗死的症状<sup>[5]</sup>,但是关于心肌梗死患者实施 PCI 后给予复方丹参滴丸的研究较少。本研究选取老年心肌梗死患者作为研究对象,探讨经皮冠状动脉介入治疗(PCI)术后心率变异性的变化及实施 PCI 治疗后给予丹参滴丸的临床疗效。

\* 基金项目:辽宁省科学技术计划项目(20120020)

作者简介:欧更(1987-),男,博士,药师,研究方向:临床药学,电话:15840100693

(收稿日期:2016-07-25 接受日期:2016-08-21)

## 1 资料与方法

### 1.1 临床资料

选取 2015 年 3 月到 2016 年 3 月因急性心肌梗死前来就诊的患者 56 例,纳入标准:①符合美国心脏病协会和美国心脏协会(ACC/AHA)制定的急性心肌梗死(AMI)治疗指南中的诊断标准;②患者同意行 PCI 治疗;③发病时间在 12 小时以内;④年龄 60~75 岁;排除标准:①凝血功能障碍;②活动性出血患者;③近一年内有重大手术或外伤;④有出血性脑卒中或严重脑血管疾病;⑤心源性休克。

依照随机数字表法将 56 例入选者分成两组, 试验组 28 例,男女比为 16/12,平均年龄(68.07±7.04)岁,其中前壁及下壁心梗分别为 13 例及 7 例,其他部位心梗 8 例,根据 Killip 分级法评定入选者心功能状况,心功能分级 I 级 3 例,II 级 7 例,III 级以上 18 例;对照组 28 例,男女比为 15/13,平均年龄(68.24±7.10)岁,其中前壁及下壁心梗分别为 15 例及 6 例,其他部位心梗 7 例,心功能分级 I 级 4 例,II 级 5 例,III 级以上 19 例。两组入选者一般资料无统计学差异(P>0.05),具有可比性。

### 1.2 治疗方法

对所有收治的患者均实施 PCI 术,术前口服给予阿司匹林(拜耳医药保健有限公司,国药准字 J20130078)300 mg 及氯吡格雷(赛诺菲制药有限公司,国药准字 J20130083)300 mg,行冠状动脉造影,同时结合体表心电图,行 PCI 术解除冠状动脉狭窄,术后对照组采取药物治疗,给予患者硝酸酯类药物,静脉滴注硝酸甘油(山东华信制药集团股份有限公司,国药准字 H37021469)10 μg/min,可酌情增加剂量,直至 ABP 降低 30 mmHg,给药时间为 48 小时;由于溶栓治疗对于急性心肌梗死尤为重要,因此行抗血小板治疗,PCI 术后第二天给予阿司匹林 200 mg/d,三天后改为小剂量 100 mg/d;同时给予β受体阻断剂,使 MCF 下降,保护心肌细胞,美托洛尔(威特药业有限公司,国药准字 H20123193)口服给药 25 mg/次,每日两次,以及血管紧张素酶抑制剂使心肌重塑,卡托普利(上海青平药业有限公司,国药准字 H31020697)口服给药 12.5 mg/次,每日两

次;同时治疗期间及时纠正电解质紊乱及酸碱平衡失调;上述给药共持续 3 个月。试验组除上述治疗外,增加使用由天士力制药公司生产的复方丹参滴丸,口服 10 丸每次,每日三次,共治疗 3 个月。

### 1.3 观察指标

**1.3.1 心率变异性** 分别检测患者 PCI 术前、术后 1 周及术后三个月的心率变异性(HRV)。采用 DHD-6000 心率变异性检测仪检测。心率变异性通常对时域及频域相关指标进行测定。时域测定以 RR 间期的变异为基础,主要检测 SDNN (所有窦性 RR 间期的标准差)、SDNN Index(每 5 min 窦性 RR 间期标准差均值)、SDANN(每 5 min 窦性 RR 间期均值的标准差),单位为 ms。频域测定是把心率定量转化为频率的形成表现出来,主要指标有高频带(HF,0.15-0.40 Hz,由迷走神经介导)、低频带(LF,0.04-0.15 Hz,由交感神经、迷走神经共同介导)、LF/HF(评价交感-迷走神经张力是否达到平衡),单位为 ms<sup>2</sup>。

**1.3.2 心功能检测** 对患者治疗前后行超声心动图检测,分别记录治疗前后血流动力学的变化,主要观察指标有心脏指数(CI)、每搏输出量(SV)、左心室射血分数(LVEF)、左心室舒张末径(LVEDD)。

### 1.4 统计学分析

所得结果输入 SPSS17.0 软件中整理分析,上述观察指标均采用 Mean±SD 表示,选择 t 检验统计分析,以 P<0.05 记为差异有统计学意义。

## 2 结果

### 2.1 老年心肌梗死患者 PCI 术前后心率变异性的变化

PCI 术后一周及术后三个月时域测定指标 SDNN、SDNN Index 及 SDANN 相对于术前均有升高(P<0.05),而术后一周及术后三个月比较无统计学差异(P>0.05);PCI 术后一周及术后三个月频域分析指标 HF 及 LF 相对于术前均升高,LF/HF 比值降低(P<0.05),而术后一周及术后三个月比较无统计学差异(P>0.05),见表 1。

表 1 老年心肌梗死患者 PCI 术前后心率变异性的变化( $\bar{x} \pm s$ )

Table 1 Changes of HRV parameters of elderly patients with myocardial infarction before and after PCI treatment( $\bar{x} \pm s$ )

| Indexes              | Preoperative | One week after surgery | Three months after operation |
|----------------------|--------------|------------------------|------------------------------|
| SDNN(ms)             | 115.20±21.05 | 125.28±20.33*          | 127.07±21.55*                |
| SDNN Index(ms)       | 48.32±11.65  | 55.05±10.50*           | 55.43±9.37*                  |
| SDANN(ms)            | 103.51±15.67 | 110.26±12.55*          | 111.20±11.35*                |
| HF(ms <sup>2</sup> ) | 40.33±8.36   | 52.30±9.12*            | 52.75±9.40*                  |
| LF(ms <sup>2</sup> ) | 53.75±6.33   | 58.72±7.69*            | 59.16±8.29*                  |
| LF/HF                | 1.34±0.34    | 1.120±0.27*            | 1.10±0.23*                   |

Note: Compared with before operation, \*P<0.05.

### 2.2 两组治疗前后心功能的比较

治疗前,两组患者的心功能指标 LVEF、LVEDD、SV、CI 比较均无明显差异(P>0.05);治疗 3 个月后,所有参与试验者 LVEF、SV 及 CI 均提高,LVEDD 降低(P<0.05),但是与对照组相比,试验组患者 LVEF、SV 及 CI 较高,LVEDD 较低(P<0.

05),表明试验组心功能恢复更好,临床效果显著,见表 2。

## 3 讨论

心肌梗死是在冠状动脉粥样硬化的基础上发生的由于斑块破裂形成血栓,导致冠状动脉闭塞,发生心肌损伤的心血管

表 2 两组患者治疗前后心功能指标比较( $\bar{x} \pm s$ )Table 2 Comparison of the cardiac function indexes between two groups before and after treatment( $\bar{x} \pm s$ )

| Indexes                   | Experiment group(n=28) |                 | Control group(n=28) |                 |
|---------------------------|------------------------|-----------------|---------------------|-----------------|
|                           | Before treatment       | After treatment | Before treatment    | After treatment |
| LVEF(%)                   | 47.33± 7.15            | 61.39± 5.41*#   | 47.26± 6.85         | 56.02± 5.67*    |
| LVEDD(mm)                 | 57.12± 8.65            | 46.33± 6.10*#   | 57.66± 7.28         | 52.05± 6.48*    |
| SV(mL)                    | 62.41± 5.56            | 79.05± 6.48*#   | 62.83± 5.94         | 71.24± 6.07*    |
| CI(L/min/m <sup>2</sup> ) | 3.67± 1.76             | 5.80± 1.69*#    | 3.58± 1.82          | 4.91± 1.78*     |

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

疾病,致死率极高<sup>[6]</sup>。由于药物治疗远期疗效不确定,使得再灌注治疗成为治疗心肌梗死的重要手段之一,而 PCI 可以使冠状动脉恢复血流,提高左心室功能,使心肌细胞周围血管再次充盈,保护心肌细胞,对心肌梗死患者有明显的治疗作用<sup>[7-9]</sup>。

本研究中选取心率变异性作为评价心脏自主神经功能的无创性指标,可评价神经体液因素与窦房结之间的联系,进而反映循环系统的功能<sup>[10]</sup>。通过时域测定法测定 SDNN,进而反映 24 小时 HRV 的总和,SDNN 值越高,发生猝死的危险性越低;通过频域分析法测定高频带及低频带,其中低频带数值受交感及迷走神经影响,可以灵敏判断交感神经张力;高频带则可灵敏判断迷走神经张力,而 LF/HF 是反映两者平衡的重要指标,比值较大则以交感神经支配为主,反之以迷走神经支配为主,通过上述时域测定法及频域分析法能够很好的描述心率变异性<sup>[11-14]</sup>。在本研究中,PCI 术后一周及术后三个月时域测定指标 SDNN,SDNN Index 及 SDANN 相对于术前均有升高,说明 PCI 术可改善 HRV,降低患者发生猝死的可能性;PCI 术后一周及术后三个月时域分析指标 HF 及 LF 相对于术前均升高,LF/HF 比值降低,说明 PCI 术后心肌功能的恢复可能与降低交感神经活性,增加迷走神经张力有关。

中草药复方丹参滴丸主要由丹参、三七及冰片组成,具有通畅血脉的功效,近年来研究显示其具有扩张冠状动脉、抗血小板凝集等功效,能够缓解急性心肌梗死的症状<sup>[15-17]</sup>。其机制可能为调节内皮活性物质血栓素、前列环素等表达,从而调节血管收缩功能<sup>[18]</sup>;抗血小板聚集;抑制内皮素分泌;抵抗钙超载;维持线粒体功能以及抗炎、抗氧化的作用<sup>[19-20]</sup>。本研究结果显示治疗 3 个月后,所有参与试验者 LVEF、SV 及 CI 均提高,LVEDD 降低,与基础药物治疗的患者相比,采用基础药物同时联合使用复方丹参滴丸的患者 LVEF、SV 及 CI 较高,LVEDD 较低,说明复方丹参滴丸对于 PCI 术后的循环系统功能恢复较好,临床效果显著。

综上所述,PCI 术能够改善老年心肌梗死患者心率变异性,而复方丹参滴丸 PCI 术后老年心肌梗死患者心功能指标均有明显改善,临床疗效较好。

#### 参考文献(References)

- [1] Cheng C L, Lee C H, Chen P S, et al. Validation of acute myocardial infarction cases in the national health insurance research database in taiwan[J]. Journal of Epidemiology, 2014, 24(6): 500-507
- [2] Hernandez I, Baik S H, Piñera A, et al. Risk of bleeding with dabigatran in atrial fibrillation [J]. JAMA internal medicine, 2015, 175(1):

18-24

- [3] Iturra S A, Suri R M, Greason K L, et al. Outcomes of surgical aortic valve replacement in moderate risk patients: implications for determination of equipoise in the transcatheter era[J]. The Journal of thoracic and cardiovascular surgery, 2014, 147(1): 127-132
- [4] Chanti-Ketterl M, Pathak E B, Andel R, et al. Dementia: a barrier to receiving percutaneous coronary intervention for elderly patients with ST-elevated myocardial infarction[J]. International journal of geriatric psychiatry, 2014, 29(9): 906-914
- [5] Mayeda E R, Karter A J, Huang E S, et al. Racial/ethnic differences in dementia risk among older type 2 diabetic patients: The diabetes and aging study[J]. Diabetes care, 2014, 37(4): 1009-1015
- [6] Falk R H, Quarta C C, Dorbala S. How to image cardiac amyloidosis [J]. Circulation: Cardiovascular Imaging, 2014, 7(3): 552-562
- [7] Barnes D E, Kaup A, Kirby K A, et al. Traumatic brain injury and risk of dementia in older veterans[J]. Neurology, 2014, 83(4): 312-319
- [8] Meziab O, Kirby K A, Williams B, et al. Prisoner of war status, post-traumatic stress disorder, and dementia in older veterans [J]. Alzheimer's & Dementia, 2014, 10(3): S236-S241
- [9] Castaño A, Bokhari S, Maurer M S. Could late enhancement and need for permanent pacemaker implantation in patients undergoing TAVR be explained by undiagnosed transthyretin cardiac amyloidosis? [J]. Journal of the American College of Cardiology, 2015, 65(3): 311-312
- [10] Mattila O S, Sairanen T, Laakso E, et al. Cerebral amyloid angiopathy related hemorrhage after stroke thrombolysis: case report and literature review[J]. Neuropathology, 2015, 35(1): 70-74
- [11] Maurer M S. Noninvasive identification of ATTRwt cardiac amyloid: the re-emergence of nuclear cardiology [J]. The American journal of medicine, 2015, 128(12): 1275-1280
- [12] Xu Y, Yang Y, Luo Y Q. Effect of atorvastatin on serum oxidative stress and N-terminal brain natriuretic peptide expression in rats[J]. Asian Pacific journal of tropical medicine, 2014, 7(5): 398-401
- [13] Zhang X, Lu J, Zhang S, et al. Effects of simulated heat waves on cardiovascular functions in senile mice [J]. International journal of environmental research and public health, 2014, 11(8): 7841-7855
- [14] Deux J F, Mihalache C I, Legou F, et al. Noninvasive detection of cardiac amyloidosis using delayed enhanced MDCT: a pilot study[J]. European radiology, 2015, 25(8): 2291-2297
- [15] Wang T L. Statin (Mevalotin) preconditioning decreases infarct size in senile rat myocardial infarction model [J]. Journal of Acute Medicine, 2014, 4(3): 127-132

- [2] Kilfoy BA, Zheng T, Holford TR, et al. International patterns and trends in thyroid cancer incidence, 1973-2002[J]. *Cancer Causes Control*, 2009, 20(5): 525-531
- [3] White ML, Doherty GM. Level VI lymph node dissection for papillary thyroid cancer[J]. *Minerva Chir*, 2007, 62(5): 383-393
- [4] Roti E, Rossi R, Trasforini G, et al. Clinical and histological characteristics of papillary thyroid microcarcinoma: results of a retrospective study in 243 patients [J]. *J Clin Endocrinol Metab*, 2006, 91(6): 2171-2178
- [5] 中华医学会内分泌学分会, 中华医学会外科学分会内分泌学组, 中国抗癌协会头颈肿瘤专业委员会, 中华医学会核医学分会. 甲状腺结节和分化型甲状腺癌诊治指南 [J]. *中华内分泌代谢杂志*, 2012, 28(10): 779-797
- Chinese Society of Endocrinology, Chinese Society of General Surgery Endocrinology Group, China Anti-Cancer Association Head and Neck Tumor Professional Committee, Chinese Society of Nuclear Medicine. Guidelines on the Diagnosis and Treatment of Thyroid Nodules and Differentiated Thyroid Carcinomas [J]. *Chin J Endocrinol Metab*, 2012, 28(10): 779-797
- [6] Ditkoff BA, Marvin MR, Yemul S, et al. Detection of circulating thyroid cells in peripheral blood[J]. *Surgery*, 1996, 120(6): 959-964, discussion 964-965
- [7] Roddiger SJ, Bojunga J, Klee V, et al. Detection of thyroid peroxidase mRNA in peripheral blood of patients with malignant and benign thyroid diseases[J]. *J Mol Endocrinol*, 2002, 29(3): 287-295
- [8] NCCN guidelines: Thyroid carcinoma[S]. Version 3, 2011
- [9] Kimura S, Kotani T, McBride OW, et al. Human thyroid peroxidase: Complete cDNA and protein sequence, chromosome mapping and identification of two alternatively spliced mRNAs[J]. *Proc Natl Acad Sci USA*, 1987, 84(16): 5555-5559
- [10] Bertaux F, Noel M, Malthiery Y, et al. Demonstration of a heterogeneous transcription pattern of thyroglobulin mRNA in human thyroid tissues[J]. *Biochem Biophys Res Com*, 1991, 178(2): 586-592
- [11] Ishikawa T, Miwa M, Uchida K. Quantitation of thyroid peroxidase mRNA in peripheral blood for early detection of thyroid papillary carcinoma[J]. *Thyroid*, 2006, 16(5): 435-442
- [12] Johnson PWM, Burchill SA, Selby PJ. The molecular detection of circulating tumour cells[J]. *Br J Cancer*, 1995, 72(2): 268-276
- [13] Ghossein RA, Bhattacharya S, Rosai J. Molecular detection of micrometastases and circulating tumor cells in solid tumors [J]. *Clin Cancer Res*, 1999, 5(8): 1950-1960
- [14] 韩静静, 吴艺捷. 外周血甲状腺肿瘤标记物的研究进展[J]. *国际内分泌代谢杂志*, 2010, 30(3): 155-158
- Han Jing-jing, Wu Yi-jie. Recent progress of thyroid tumor markers in peripheral blood[J]. *Int J Endocrinol Metab*, 2010, 30(3): 155-158
- [15] Tallini G, Ghossein RA, Emanuel J, et al. Detection of thyroglobulin, thyroid peroxidase, and RET/PTC1 mRNA transcripts in the peripheral blood of patients with thyroid disease [J]. *J Clin Oncol*, 1998, 16(3): 1158-1166
- [16] Podnos YD, Smith D, Wagman LD, et al. The implication of lymph node metastasis on survival in patients with well-differentiated thyroid cancer[J]. *Am Surg*, 2005, 71(9): 731-734
- [17] Zaydfudim V, Feurer ID, Griffin MR, et al. The impact of lymph node involvement on survival in patients with papillary and follicular thyroid carcinoma[J]. *Surgery*, 2008, 144(6): 1070-1077
- [18] Ghossein RA, Rosai J. Polymerase chain reaction in the detection of micrometastases and circulating tumor cells [J]. *Cancer*, 1996, 78(1): 10-16
- [19] Chinnappa P, Taguba L, Arciaga R, et al. Detection of thyrotropin-receptor messenger ribonucleic acid(mRNA) and thyroglobulin mRNA transcripts in peripheral blood of patients with thyroid disease: sensitive and specific markers for thyroid cancer [J]. *Clin Endocrinol Metab*, 2004, 89(8): 3705-3709
- [20] 范群, 匡安仁, 袁耿彪. 外周血甲状腺球蛋白 mRNA 对分化型甲状腺癌的诊断价值[J]. *中华核医学杂志*, 2008, 28(4): 267-269
- Fan Qun, Kuang An-ren, Yuan Geng-biao. Evaluation of thyroglobulin mRNA in peripheral blood of patients with differentiated thyroid carcinoma after remnant ablation [J]. *Chin J Nucl Med*, 2008, 28(4): 267-269

(上接第 61 页)

- [16] Prytuliak O M. Thiotriazolin Influence on Blood Pressure Changes in Patients with Myocardial Infarction and Concomitant Arterial Hypertension Who Underwent Remedial Treatment and Physical Rehabilitation[J]. *Galician Medical Journal*, 2015, 22(4): 1-4
- [17] He L, Zhang J, Yang Q, et al. The Incidence and Risk Factors of Acute Asymptomatic Brain Infarcts After Percutaneous Coronary Intervention in Patients with Acute Myocardial Infarction [J]. *International Journal of Gerontology*, 2014, 8(2): 70-73
- [18] Yadav A, SahdabRaheel M, Sharma G, et al. Cardiac tamponade due to cardiac rupture in myocardial infarction-a silent killer[J]. *Journal of Punjab Academy of Forensic Medicine & Toxicology*, 2015, 15(1): 30-33
- [19] Romila A, Nechita A, Tutunaru D. Enzymatic specificity of coronarian syndromes in elderly patients[J]. *Acta Medica Mediterranea*, 2015, 31(5): 1007-1011
- [20] Niu J, Ma Z. Influence of Cinepazide Maleate on Vascular Endothelial Function of Patients with Acute Myocardial Infarction [J]. *Advanced Emergency Medicine*, 2015, 4(3): 1-3