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伊伐布雷定联合美托洛尔对缺血性心肌病 PCI 术患者心功能、预后及血清炎性因子的影响 *

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摘要 目的:探讨伊伐布雷定联合美托洛尔对缺血性心肌病(ICM)行经皮冠状动脉介入术(PCI)术后患者心功能、预后及血清炎性因子的影响。**方法:**选取 2018 年 7 月-2019 年 4 月我院收治的行 PCI 术的 ICM 患者 98 例,将随机数字表法分为实验组与对照组,各 49 例,对照组给予美托洛尔治疗,实验组给予伊伐布雷定联合美托洛尔治疗,对比两组优良率、心功能、预后、不良反应及血清炎性因子。**结果:**实验组治疗 8 周后的优良率为 93.75%(45/48),高于对照组的 70.83%(34/48)($P<0.05$)。实验组治疗 8 周后左心室射血分数(LVEF)、6 min 步行试验(6MWT)距离高于对照组,N 末端 B 型钠尿肽原(NT-proBNP)、24 h 心率(24hHR)低于对照组($P<0.05$)。实验组治疗 8 周后肿瘤坏死因子- α (TNF- α)、超敏 C 反应蛋白(hs-CRP)、白介素-6(IL-6)低于对照组($P<0.05$)。实验组 3 个月内再住院率、3 个月内病死率低于对照组($P<0.05$)。两组不良反应发生率比较无差异($P>0.05$)。**结论:**相较于单用美托洛尔,联合伊伐布雷定治疗 PCI 术后的 ICM 患者,可更好地改善患者心功能,降低炎性因子水平,且安全性较好,改善患者预后的效果更佳。

关键词:伊伐布雷定;美托洛尔;缺血性心肌病;经皮冠状动脉介入术;心功能;预后;炎性因子

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Effects of Ivabradine Combined with Metoprolol on Cardiac Function, Prognosis and Serum Inflammatory Factors in Patients with Ischemic Cardiomyopathy Undergoing PCI*

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ABSTRACT Objective: To investigate the effect of ivabradine combined with metoprolol on cardiac function, prognosis and serum inflammatory factors in patients with ischemic cardiomyopathy (ICM) undergoing percutaneous coronary intervention (PCI). **Methods:** 98 patients with ICM undergoing PCI in our hospital from July 2018 to April 2019 were selected, and randomly divided into experimental group and control group by random number table method, 49 cases in each group. The control group was treated with metoprolol, and the experimental group was treated with ivabradine combined with metoprolol. The excellent and good rate, cardiac function, prognosis, adverse reactions and serum inflammatory factors were compared between two groups. **Results:** 8 weeks after treatment, the excellent and good rate of the experimental group was 93.75% (45/48), which was higher than 70.83% (34 / 48) of the control group ($P<0.05$). 8 weeks after treatment, left ventricular ejection fraction (LVEF) and 6-minute walk test (6MWT) distance of experimental group were higher than control group, and N-terminal pro-B-type natriuretic peptide (NT proBNP), 24h heart rate (24hHR) of experimental group were lower than those of control group ($P<0.05$). 8 weeks after treatment, the levels of tumor necrosis factor - α (TNF- α), high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) of experimental group were lower than control group ($P<0.05$). The rehospitalization rate and mortality within 3 months of the experimental group were lower than control group ($P<0.05$). There was no significant difference in incidence of adverse reactions between two groups ($P>0.05$). **Conclusion:** Compared with metoprolol alone, combined with ivabradine in the treatment of patients with ICM after PCI, can effectively improve the cardiac function, reduce the level of inflammatory factors, and has better safety, and the effect of improving the prognosis of patients is better.

Key words: Ivabradine; Metoprolol; Ischemic cardiomyopathy; Percutaneous coronary intervention; Cardiac function; Prognosis; Inflammatory factors

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前言

缺血性心肌病(ICM)属于冠心病的晚期阶段,是指由冠状动脉粥样硬化导致的长期心肌缺血,致使心肌弥漫性纤维化的一组临床综合征^[1,2]。ICM临床主要表现为扩大的心腔、心律失常以及反复发作的心力衰竭等^[3]。经皮冠状动脉介入术(PCI)是治疗ICM的常用方案,可有效恢复机体血运重建,有效改善患者预后^[4,5]。但有研究表明^[6],由于PCI血运重建过程中缺血再灌注导致缺血心肌细胞凋亡、局部炎症反应,影响心功能。因此,PCI术后给予适当的药物治疗以改善患者预后具有重要意义。美托洛尔是临床常见的 β 受体阻滞剂,可降低心肌耗氧量,改善心肌灌注,但疗效仍存在局限性^[7,8]。伊伐布雷定是临床新型的减慢心率的药物,可有效降低心率及心肌耗氧量^[9,10]。本研究选取部分于我院行PCI术的ICM患者,将其分为对照组、实验组,观察在美托洛尔基础上应用伊伐布雷定联合治疗对ICM患者PCI术后心功能、预后及血清炎症因子的影响。

1 资料与方法

1.1 一般资料

选取2018年7月-2019年4月我院收治的行PCI术的ICM患者98例,纳入标准:(1)符合《心肌病诊断与治疗建议》^[11]中关于ICM的诊断标准;(2)均符合PCI手术指征,且均成功完成手术者;(3)手术均由同一组医师完成;(4)患者及其家属签署知情同意书;(5)临床症状稳定,无急性心衰的反复发作。排除标准:(1)治疗过程中出现急性心力衰竭;(2)因为心率过慢或血压过低而停药;(3)合并重度心脏瓣膜病、扩张型心肌病、先天性心脏病;(4)心房纤颤及控制不佳的室性心律失常;(5)存在药物禁忌症者。将其按随机数字表法分为实验组与对照组,各49例,其中对照组男26例,女23例,平均年龄 (61.28 ± 4.35) 岁;平均体质指数 (23.29 ± 1.14) kg/m²;合并疾病:糖尿病6例,高血压9例,高血脂5例。实验组男28例,女21例,平均年龄 (61.93 ± 5.28) 岁;合并疾病:糖尿病8例,高血压7例,高血脂6例;平均体质指数 (23.57 ± 1.26) kg/m²。两组一般资料对比无差异($P>0.05$),均衡可比。此次研究已通过我院伦理学委员会批准。

1.2 方法

两组患者均成功行PCI术,并依据《中国经皮冠状动脉介入治疗指南2012》^[12],进行严格操作,术后常规使用双联抗血小板药物、他汀类药物治疗。在此基础上,对照组给予美托洛尔治疗,酒石酸美托洛尔片(国药准字:H32025391,阿斯利康制药有限公司生产,规格:25 mg/片),口服,25 mg/次,2次/d。实验组给予美托洛尔联合伊伐布雷定治疗,盐酸伊伐布雷定片(法国Les Laboratoires Servier生产,注册证号:H20150217,规格:5 mg/片)口服,2.5 mg/次,2次/d;美托洛尔治疗方案同对照组。两组均治疗8周。

1.3 观察指标

(1)心功能:两组患者均由2名有经验的心脏超声专业医师进行心脏超声检查,记录两组治疗前、治疗8周后的左心室射血分数(LVEF)。采集两组治疗前、治疗8周后的清晨空腹肘静脉血4 mL,室温静置0.5 h,经常规离心后分离血清置于冰箱中备用。采用美国Biosite公司提供的Triage干式快速定量法测定N末端B型钠尿肽原(NT-proBNP)。采用动态心电图(美国惠普公司生产)监测两组治疗前、治疗8周后的24 h心率(24hHR)。测定两组患者治疗前、治疗8周后的6 min步行试验(6MWT)距离。(2)参考试剂盒(上海锐赛生物技术有限公司)说明书步骤,采用双抗体夹心酶联免疫吸附法检测炎症因子指标:白介素-6(IL-6)、超敏C反应蛋白(hs-CRP)、肿瘤坏死因子- α (TNF- α)。(3)预后:所有患者均于治疗结束后随访3个月,采用电话随访方式,记录两组患者3个月内再住院率及3个月内病死率。(4)安全性评价:记录两组治疗期间不良反应情况。(5)疗效:优:心功能分级改善2级或2级以上;良:心功能分级改善1级;差:心功能分级未见改善甚至病情加重。优良率=优率+良率^[13]。

1.4 统计学方法

采用SPSS 24.0软件分析数据。以率表示计数资料,行卡方检验。以 $(\bar{x} \pm s)$ 表示计量资料,采用t检验。 $\alpha=0.05$ 为检验水准。

2 结果

2.1 两组优良率比较

实验组治疗8周后的优良率为93.75%(45/48),高于对照组的70.83%(34/48)($P<0.05$),详见表1。

表1 两组优良率比较例(%)

Table 1 Comparison of excellent and good rate between the two groups [n(%)]

Groups	Excellent	Good	Bad	Excellent and good rate
Control group(n=48)	12(25.00)	22(45.83)	14(29.17)	34(70.83)
Experimental group(n=48)	17(35.42)	28(58.33)	3(6.25)	45(93.75)
χ^2				8.649
P				0.003

2.2 两组心功能指标比较

治疗前,两组LVEF、NT-proBNP、24hHR、6MWT距离相比差异无统计学意义($P>0.05$),治疗8周后,两组LVEF、6MWT距离较治疗前升高,NT-proBNP、24hHR较治疗前降低($P<0.05$),治疗8周后实验组LVEF、6MWT较对照组高,24hHR、

NT-proBNP较对照组低($P<0.05$),详见表2。

2.3 两组炎症因子指标比较

治疗前,两组炎症因子指标相比无差异($P>0.05$),治疗8周后,两组hs-CRP、TNF- α 、IL-6较治疗前降低($P<0.05$),实验组治疗8周后hs-CRP、TNF- α 、IL-6较对照组低($P<0.05$),详见表3。

表 2 两组心功能指标比较($\bar{x} \pm s$)Table 2 Comparison of cardiac function indexes between the two groups($\bar{x} \pm s$)

Groups	LVEF(%)		NT-proBNP(pg/mL)		24hHR(beats/min)		6MWT distance(m)	
	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment
Control group (n=48)	42.11± 5.87	47.82± 6.34 ^a	5312.39± 271.83	3547.76± 294.82 ^a	93.82± 6.55	84.29± 5.24 ^a	258.28± 23.84	311.75± 30.92 ^a
Experimental group(n=48)	41.96± 6.02	54.16± 5.12 ^a	5327.05± 364.90	2594.23± 426.71 ^a	93.41± 8.71	72.64± 6.07 ^a	257.54± 19.76	375.42± 26.87 ^a
t	0.124	5.390	0.223	12.737	0.261	10.065	0.166	13.428
P	0.902	0.000	0.824	0.000	0.795	0.000	0.869	0.000

Note: compared with before treatment, ^a $P < 0.05$.

表 3 两组炎症因子指标比较($\bar{x} \pm s$)Table 3 Comparison of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	hs-CRP(mg/L)		TNF- α (pg/mL)		IL-6(ng/L)	
	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment	Before treatment	8 weeks after treatment
Control group (n=48)	21.53± 4.17	15.08± 4.29 ^a	580.34± 36.92	437.62± 24.88 ^a	26.34± 4.21	19.23± 2.64 ^a
Experimental group (n=48)	21.18± 5.16	8.33± 2.25 ^a	582.77± 33.89	225.78± 23.74 ^a	26.19± 6.78	13.21± 2.88 ^a
t	0.366	9.654	0.336	42.679	0.130	12.492
P	0.716	0.000	0.738	0.000	0.897	0.000

Note: compared with before treatment, ^a $P < 0.05$.

2.4 两组不良反应比较

两组不良反应发生率比较无差异($P > 0.05$),详见表 4。

随访 3 个月无失访病例。实验组 3 个月内再住院率、3 个月

内病死率低于对照组($P < 0.05$),详见表 5。

2.5 两组预后指标比较

表 4 两组不良反应发生率比较 [例(%)]

Table 4 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	Bradycardia	Stomach discomfort	Hallucination	Total incidence rate
Control group(n=48)	2(4.17)	3(6.25)	1(2.08)	6(12.50)
Experimental group(n=48)	2(4.17)	1(2.08)	1(2.08)	4(8.33)
χ^2				0.447
P				0.504

表 5 两组预后指标比较 [例(%)]

Table 5 Comparison of prognostic indexes between the two groups [n(%)]

Groups	Rehospitalization rate within 3 months	Mortality within 3 months
Control group(n=48)	13(27.08)	9(18.75)
Experimental group(n=48)	4(8.33)	2(4.17)
χ^2	4.376	5.031
P	0.036	0.025

3 讨论

ICM 是冠心病的主要表现形式,也是导致冠心病患者死亡的主要原因^[14]。当 ICM 患者发病时,心肌细胞大量坏死和凋亡,

左心室出现病理性重构,从而引起病理性肥大;同时在二尖瓣反流、心室扩大等情况出现后,又可进一步发展为心力衰竭^[15-17]。以往有临床实践证实^[18],针对 ICM 患者给予早期再灌注治疗措施可有效提高患者生存率。PCI 是临床治疗 ICM 的常见介入术

式,可有效恢复血运,血运重建可挽救冬眠心肌或顿抑心肌细胞,使心肌细胞不至于因缺血而凋亡,改善其收缩及舒张功能,使患者生存率升高^[19]。尽管 PCI 可有效改善 ICM 患者的预后,但 PCI 的治疗效果仍会受到再灌注损伤的影响,仍有相当一部分患者在 PCI 术后可出现心力衰竭、心脏扩大以及心律失常等^[20]。此外,PCI 血运重建过程中产生的再灌注损伤还可导致钙离子、氧自由基的平衡失调,诱导缺血心肌的炎症反应,机体心功能恢复受到影响^[21,22]。因此,对 PCI 术后患者给予改善心功能、降低炎症反应的药物治疗具有积极的临床意义。美托洛尔是常见的 β 受体阻滞剂,可通过抑制交感神经过度激活、减慢心率等对心肌细胞产生抑制作用,降低死亡率与主要心脏事件发生率,同时美托洛尔还有抗氧化、抗心肌细胞凋亡作用^[23,24]。但由于 β 受体阻滞剂会受到严重心动过缓、低血压、心肺功能等影响,难以达到预期治疗效果,亟待寻找更有效的联合药物治疗方法。

伊伐布雷定是心力衰竭的常用药物,用于 PCI 术后的 ICM 患者可有效降低心率,而心率的降低可以进一步减少心肌耗氧,改善心肌供血,促进心功能改善^[25]。本研究中,实验组的心功能改善效果优于对照组,且优良率相对更高,表明相较于单用美托洛尔,联合伊伐布雷定治疗 PCI 术后的 ICM 患者,疗效更为显著。伊伐布雷定作为拥有特异性抑制心脏起搏 If 电流的药物,可作用于窦房结细胞来使心率减慢,并对机体心脏传导及心肌收缩力影响较小,可克服美托洛尔的不良作用^[26]。同时伊伐布雷定具有抗炎、抑制心肌重构、抑制动脉粥样硬化斑块形成等多重药理作用^[27]。国内外不少研究亦证实^[28,29],伊伐布雷定可有效改善患者心功能,改善患者心率失常。本次研究结果还显示,实验组治疗 8 周后 hs-CRP、TNF- α 、IL-6 低于对照组,提示伊伐布雷定可通过抑制机体炎症反应,从而减少心肌炎性因子浸润,可能是抑制机体心肌重构的主要作用机制之一。对比两组不良反应发生率可知,两组治疗方案均安全可靠,患者易于接受。另实验组 3 个月内再住院率、3 个月内病死率低于对照组,表明美托洛尔联合伊伐布雷定可有效改善患者预后,可能与该治疗方案可促进患者心功能恢复、减轻炎症反应,降低缺血再灌注损伤,从而改善患者整体机能有关^[30]。值得注意的是,本研究仅分析了伊伐布雷定与美托洛尔联合治疗,对于其他联合用药方案仍有待进一步验证。此外,本研究样本量偏小,随访时间较短,实验数据的准确性还具有提升空间。

综上所述,相较于单用美托洛尔,联合伊伐布雷定治疗 PCI 术后的 ICM 患者,可更有效地改善患者心功能,降低炎症因子水平,且安全性较好,改善患者预后效果更佳。

参考文献(References)

- [1] Pandozi C, Lavallo C, Russo M, et al. Mapping of ventricular tachycardia in patients with ischemic cardiomyopathy: Current approaches and future perspectives[J]. Clin Cardiol, 2019, 42(10): 1041-1050
- [2] Sharma S, Sharma R, Lardizabal J. Myocardial Viability and Long-Term Outcomes in Ischemic Cardiomyopathy[J]. N Engl J Med, 2019, 381(24): 2373
- [3] Napp LC, Bengel FM, Bauersachs J. Myocardial Viability and Long-Term Outcomes in Ischemic Cardiomyopathy[J]. N Engl J Med, 2019, 381(24): 2373
- [4] Rudas L, Zima E. Coronary angiography and percutaneous intervention after resuscitation[J]. Orv Hetil, 2019, 160(46): 1826-1831
- [5] Dalgaard F, Jones WS, Piccini JP. Atrial Fibrillation and Percutaneous Coronary Intervention [J]. Circ Cardiovasc Interv, 2019, 12 (8): e008269
- [6] Khan MR, Kayani WT, Ahmad W, et al. Effect of increasing age on percutaneous coronary intervention vs coronary artery bypass grafting in older adults with unprotected left main coronary artery disease: A meta-analysis and meta-regression [J]. Clin Cardiol, 2019, 42 (11): 1071-1078
- [7] Bayer O, Adrion C, Al Tawil A, et al. Results and lessons learnt from a randomized controlled trial: prophylactic treatment of vestibular migraine with metoprolol(PROVEMIG)[J]. Trials, 2019, 20(1): 813
- [8] Qin W, Zhang L, Li Z, et al. Metoprolol protects against myocardial infarction by inhibiting miR-1 expression in rats[J]. J Pharm Pharmacol, 2020, 72(1): 76-83
- [9] Seo Y, Ohte N. Effects of Heart Rate Reduction by Ivabradine for Heart Failure Beyond β -Blockers[J]. Circ J, 2019, 83(10): 1991-1993
- [10] Sumarsono A, Vaduganathan M, Ajufu E, et al. Contemporary Patterns of Medicare and Medicaid Utilization and Associated Spending on Sacubitril/Valsartan and Ivabradine in Heart Failure [J]. JAMA Cardiol, 2019, 5(3): 336-339
- [11] 中华医学会心血管病学分会, 中华心血管病杂志编辑委员会, 中国心肌病诊断与治疗建议工作组. 心肌病诊断与治疗建议 [J]. 中华心血管病杂志, 2007, 35(1): 5-16
- [12] 中华医学会心血管病学分会介入心脏病学组, 中国医师协会心血管内科医师分会血栓防治专业委员会, 中华心血管病杂志编辑委员会. 中国经皮冠状动脉介入治疗指南(2016)[J]. 中华心血管病杂志, 2016, 44(5): 382-400
- [13] 周洪伟, 张冰, 赵海鸿, 等. PCI 术对心肌梗死患者的疗效及 Hcy、I-MA、hs-CRP 的变化研究[J]. 中国急救复苏与灾害医学杂志, 2019, 14(11): 1042-1044
- [14] Yamamoto R, Miyagawa S, Toda K, et al. Long-Term Outcome of Ischemic Cardiomyopathy After Autologous Myoblast Cell-Sheet Implantation[J]. Ann Thorac Surg, 2019, 108(5): e303-e306
- [15] Bhaskaran A, De Silva K, Rao K, et al. Ventricular Tachycardia Ablation in Non-ischemic Cardiomyopathy [J]. Korean Circ J, 2020, 50 (3): 203-219
- [16] Yi X, Jiang DS, Feng G, et al. An altered left ventricle protein profile in human ischemic cardiomyopathy revealed in comparative quantitative proteomics[J]. Kardiol Pol, 2019, 77(10): 951-959
- [17] 贾玲玲, 余平, 陈帆, 等. 缺血性心脏病患者血浆 microRNA-21 的表达及作用机制研究 [J]. 现代生物医学进展, 2018, 18 (1): 78-81, 116
- [18] Seferović PM, Polovina MM, Coats AJS. Heart failure in dilated non-ischaemic cardiomyopathy[J]. Eur Heart J Suppl, 2019, 21(Suppl M): M40-M43
- [19] Symons JD, Deeter L, Deeter N, et al. Effect of Continuous-Flow Left Ventricular Assist Device Support on Coronary Artery Endothelial Function in Ischemic and Nonischemic Cardiomyopathy [J]. Circ Heart Fail, 2019, 12(8): e006085
- [20] Wang Z, Song Y, A G, et al. Role of Hydration in Contrast-Induced Nephropathy in Patients Who Underwent Primary Percutaneous Coronary Intervention[J]. Int Heart J, 2019, 60(5): 1077-1082

- [8] Kim J R, Kim B M, Kim Y M, et al. Colonic Metastasis Presenting as an Intraluminal Fungating Mass 8 Years After Surgery for Ovarian Cancer[J]. *Annals of Coloproctology*, 2015, 31(5): 198-201
- [9] 蔡鸿宁, 张蕾, 张敦兰, 等. 人工神经网络在宫颈癌预后预测中的应用[J]. *肿瘤防治研究*, 2012, 39(9): 1117-1119
- [10] Xingyu, Zhu, Nan, et al. An Overview of the Application of Artificial Neural Networks in Lung Cancer Research [J]. *Chinese Journal of Lung Cancer*, 2019, 22(4): 245-249
- [11] Chavarino C P, Lecea J M S M D. Artificial neural networks in Neurosciences[J]. *Psicothema*, 2011, 23(4): 738-744
- [12] V Renganathan. Overview of artificial neural network models in the biomedical domain[J]. *Bratisl Lek Listy*, 2019, 120(7): 536-540
- [13] Donach M, Yu Y, Artioli G, et al. Combined use of biomarkers for detection of ovarian cancer in high-risk women [J]. *Tumour Biol*, 2010, 31(3): 209-215
- [14] 马超, 边云, 陆建平. 人工智能在胰腺肿瘤成像中的应用及挑战[J]. *中华胰腺病杂志*, 2019, 19(5): 343-346
- [15] 孔梓任, 王裕, 马文斌, 等. 癌症筛查在中国的开展前景[J]. *中国医药导报*, 2018, 15(9): 173-177
- [16] 吴菲, 刘霄宇, 赵根明, 等. 癌症筛查成本效果评估的研究进展[J]. *中国肿瘤*, 2016, 25(2): 81-87
- [17] 张超杰, 喻洁. 浅谈我国癌症筛查的利弊 [J]. *医学与哲学*, 2020, 1(1): 5-10
- [18] 刘昊, 牛明玥, 杨晨曦. 癌症早期筛查与过度诊断[J]. *医学与哲学*, 2020, 1(1): 11-13
- [19] Nossov V, Amneus M, Su F, et al. The early detection of ovarian cancer: from traditional methods to proteomics. Can we really do better than serum CA-125?[J]. *American Journal of Obstetrics & Gynecology*, 2008, 199(3): 215-223
- [20] Qu Y, He Y, Li Z, et al. Constructing an ovarian cancer metastasis index by dissecting medical records [J]. *Oncotarget*, 2017, 8 (60): 102212-102222
- [21] 郭俊英, 廖沁园. 卵巢癌的分子标志物及靶向治疗研究进展 [J]. *世界最新医学信息文摘*, 2019, 9(96): 88-89
- [22] Yang Z J, Zhao B B, Li L. The significance of the change pattern of serum CA125 level for judging prognosis and diagnosing recurrences of epithelial ovarian cancer [J]. *Journal of Ovarian Research*, 2016, 9 (1): 57
- [23] Yuan Q, Song J, Yang W, et al. The effect of CA125 on metastasis of ovarian cancer: old marker new function[J]. *Oncotarget*, 2017, 8(30): 50015-50022
- [24] 吴志浩, 魏祥松, 汤汇明, 等. 血清前白蛋白测定在恶性肿瘤中的临床应用 [J]. *国外医学 (临床生物化学与检验学分册)*, 2005, 7(10): 759-760
- [25] Kozak KR, Su F, Whitelegge JP, et al. Characterization of serum biomarkers for detection of early stage ovarian cancer[J]. *Proteomics*, 2005, 5(17): 4589-4596
- [26] 牛星燕, 张冬萍, 李飞霞, 等. 卵巢恶性肿瘤化疗研究进展[J]. *国际妇产科学杂志*, 2020, 2(2): 125-128
- [27] 赖影. 不同方法治疗卵巢癌的效果及对患者生存质量的影响比较 [J]. *中国当代医药*, 2020, 1(2): 110-113
- [28] Kim S, Kim B, Song YS. Ascites modulates cancer cell behavior, contributing to tumor heterogeneity in ovarian cancer [J]. *Cancer Sci*, 2016, 107(9): 1173-1178
- [29] MikulA-Pietrasik J, Uruski P, Szubert S, et al. Malignant ascites determine the transmesothelial invasion of ovarian cancer cells[J]. *International Journal of Biochemistry & Cell Biology*, 2017, 5(92): 6-13
- [30] Weidle UH, Birzele F, Kollmorgen G, et al. Mechanisms and Targets Involved in Dissemination of Ovarian Cancer [J]. *Cancer Genomics Proteomics*, 2016, 13(6): 407-423

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- [21] Wu J, Zhao L, Lin K, et al. Chinese Herbal Medicines for Restenosis After Percutaneous Coronary Intervention: A Meta-Analysis of Randomized Controlled Trials [J]. *J Altern Complement Med*, 2019, 25 (10): 983-992
- [22] Holmes DR Jr, Barsness GW. Percutaneous Coronary Intervention for Chronic Total Occlusions [J]. *Circ Cardiovasc Interv*, 2019, 12(8): e008321
- [23] Wu L, Zhang Q, Shu Q, et al. Sex-dependent changes in physical, mental, and quality of life outcomes in metoprolol-treated Chinese chronic heart failure patients[J]. *Medicine (Baltimore)*, 2019, 98(50): e18331
- [24] Meloche M, Khazaka M, Kassem I, et al. CYP2D6 polymorphism and its impact on the clinical response to metoprolol: A systematic review and meta-analysis [J]. *Br J Clin Pharmacol*, 2020, 86 (6): 1015-1033
- [25] Lee MC, Bond S, Wheeler D, et al. A randomised, double-blind, placebo-controlled crossover trial of the influence of the HCN channel blocker ivabradine in a healthy volunteer pain model: an enriched population trial[J]. *Pain*, 2019, 160(11): 2554-2565
- [26] Perissinotti L, Guo J, Kudaibergenova M, et al. The Pore-Lipid Interface: Role of Amino-Acid Determinants of Lipophilic Access by Ivabradine to the hERG1 Pore Domain [J]. *Mol Pharmacol*, 2019, 96 (2): 259-271
- [27] Banavalikar B, Shenthur J, Padmanabhan D, et al. Clinical and Electrophysiological Correlates of Incessant Ivabradine-Sensitive Atrial Tachycardia[J]. *Circ Arrhythm Electrophysiol*, 2019, 12(8): e007387
- [28] Chiu MH, Howlett JG, Sharma NC. Initiation of ivabradine in cardiogenic shock[J]. *ESC Heart Fail*, 2019, 6(5): 1088-1091
- [29] 柯贤进, 徐宏伟, 曾彬. 伊伐布雷定联合芪苈强心胶囊治疗老年缺血性心肌病的临床疗效及对炎症因子水平的影响[J]. *武汉大学学报(医学版)*, 2019, 40(6): 1008-1012
- [30] Bouabdallaoui N, O'Meara E, Bernier V, et al. Beneficial effects of ivabradine in patients with heart failure, low ejection fraction, and heart rate above 77 b.p.m[J]. *ESC Heart Fail*, 2019, 6(6): 1199-1207