doi: 10.13241/j.cnki.pmb.2020.17.045

氨氯地平联合厄贝沙坦治疗老年糖尿病伴高血压的疗效及对糖脂代谢和心肌损伤指标的影响 *

李 瑞 余本富 刘永菊 郝娜娜 吕丽娟

（安徽医科大学附属阜阳医院内分泌科 安徽 阜阳 236000）

摘要 目的：探讨氨氯地平联合厄贝沙坦治疗老年糖尿病伴高血压的疗效及对糖脂代谢和心肌损伤指标的影响。**方法：**选择我院2017年9月~2019年12月收治的98例老年糖尿病伴高血压患者，依据随机数字表法分为对照组和治疗组，每组各49例。对照组给予氨氯地平治疗，治疗组在对照组的基础上联合厄贝沙坦治疗，对比两组的临床疗效，治疗前后血压、血糖、血脂、心肌损伤指标的变化以及不良反应的发生情况。**结果：**治疗后，治疗组显效率为67.35%，显著高于对照组，差异有统计学意义（$P<0.05$）。治疗后，两组收缩压、舒张压、空腹血糖、糖化血红蛋白、总胆固醇、三油甘酯、心肌肌钙蛋白I、肌酸激酶同工酶、乳酸脱氢酶水平均较治疗前明显下降，且治疗组以上指标均明显低于对照组（$P<0.05$）。两组不良反应总发生率比较差异无统计学意义（$P>0.05$）。**结论：**氨氯地平联合厄贝沙坦能够提高老年糖尿病伴高血压的效果，改善糖脂代谢及减轻心肌损伤。

关键词：老年糖尿病伴高血压；氨氯地平；厄贝沙坦；疗效；糖脂代谢；心肌损伤

中图分类号：R587.2；R544.1 **文献标识码：**A **文章编号：**1673-6273(2020)17-3396-05

Efficacy of Amlodipine Combined with Irbesartan in the Treatment of Senile Diabetes with Hypertension and Its Effect on the Glucose and Lipid Metabolism and Myocardial Injury Indexes*

LI Rui, YU Ben-fu, LIU Yong-ju, HAO Na-na, LV Li-juan

(Department of Endocrinology, Fuyang Hospital, Anhui Medical University, Fuyang, Anhui, 236000, China)

ABSTRACT Objective: To investigate the curative effect of amlodipine combined with irbesartan on senile diabetes with hypertension and its influence on glucose and lipid metabolism and myocardial injury index. **Methods:** 98 elderly diabetic patients with hypertension admitted to our hospital from September 2017 to December 2019 were selected and divided into control group and treatment group according to random number table method, 49 cases in each group. The control group was treated with amlodipine, while the treatment group was treated with irbesartan on the basis of the control group. The clinical efficacy, changes of blood pressure, blood sugar, blood lipid, myocardial injury index before and after treatment, and the occurrence of adverse reactions were compared between the two groups **Results:** After treatment, the effective rate of the treatment group was 67.35%, which was significantly higher than that of the control group ($P<0.05$). After treatment, the levels of systolic blood pressure, diastolic blood pressure, fasting blood glucose, glycosylated hemoglobin, total cholesterol, triglyceride, cardiac troponin I, creatine kinase isoenzyme and lactate dehydrogenase in the two groups were significantly lower than those in the control group ($P<0.05$). There was no significant difference in the total incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Amlodipine combined with irbesartan can improve the effect of senile diabetes with hypertension, improve glucose and lipid metabolism and alleviate myocardial injury.

Key words: Elderly diabetes mellitus with hypertension; Amlodipine; Irbesartan; Efficacy; Glycolipid metabolism; Myocardial injury

Chinese Library Classification(CLC): R587.2; R544.1 Document code: A

Article ID: 1673-6273(2020)17-3396-05

前言

糖尿病为慢性代谢性疾病，随着近年来人口老龄化的加速及生活方式的改变，其发生率呈上升趋势，以糖代谢异常为主要特点[1,2]。随着糖尿病的进展容易合并多种慢性并发症，研究表明[3,4]糖尿病患者的高血压发生率明显高于血糖正常者。Lee JY等[5]研究表明糖尿病能够导致患者血压上升，同时血压上升又可加速糖尿病的恶化，造成恶性循环，增加临床治疗难度。厄贝沙坦属血管紧张素Ⅱ受体抑制剂，可抑制血管紧张素Ⅰ转化至血管紧张素Ⅱ，抑制血管收缩及醛固酮释放，具有显著的降压作用[6]。氨氯地平属钙离子拮抗剂，其可阻断平滑肌的钙通道，降低细胞内钙离子含量，扩张外周小动脉，降低外周阻力[7]。

* 基金项目：安徽省卫生和计划生育委员会科研计划项目(2016QK006)

作者简介：李瑞（1985-），女，本科，主治医师，研究方向：糖尿病、甲状腺等代谢病方向，E-mail: xhempy@163.com，电话：13956751897

（收稿日期：2020-05-07 接受日期：2020-05-31）

目前,有关厄贝沙坦联合氨氯地平在糖尿病伴高血压治疗中的报道较多,但相关作用机制尚不完全明确。临床研究表明[8,9]高血压患者并发糖代谢异常后心血管并发症的风险明显增加。心肌指标能够直观反映心肌情况,也可反映糖尿病伴高血压患者心肌损伤程度。心肌肌钙蛋白 I(Cardiac troponin i,cTnI)、肌酸激酶同工酶(creatine kinase-Isoenzyme,CK-MB)及乳酸脱氢酶(Lactate dehydrogenase,LDH)为常见心肌酶,具有显著的敏感性,在心肌损伤时以上指标能够在短时间内上升,可反应心肌损伤程度。本研究旨在分析氨氯地平联合厄贝沙坦治疗老年糖尿病伴高血压疗效及对患者糖脂代谢和心肌损伤的影响。

1 资料与方法

1.1 一般资料

选择 98 例老年糖尿病伴高血压患者,纳入标准:既往已确诊为 2 型糖尿病,且符合高血压诊断标准[10]:血压持续或≥ 3 次非同日坐位收缩压 (Systolic blood pressure,SBP)≥ 140 mmHg 或舒张压(Diastolic pressure,DBP)≥ 90 mmHg;年龄≥ 60 岁。排除标准:肝肾功能不全;入组前 1 周内接受胰岛素及降压药;近期有心力衰竭、脑卒中等疾病。依据随机数字表法将患者分为对照组和治疗组,每组各 49 例。对照组年龄(68.94± 2.75)岁;女 26 例, 男 23 例; 糖尿病病程 (10.52± 1.39) 年; 高血压病程(6.81± 1.46) 年; 平均体质量 (64.18± 5.11)kg。治疗组年龄(67.65± 2.94)岁;女 29 例,男 20 例;糖尿病病程(11.04± 1.64)年;高血压病程(7.02± 1.32)年;平均体质量(65.29± 4.96)kg。两组基线资料比较无统计学差异(P>0.05),具有可比性。

1.2 治疗方法

两组患者治疗期间均积极控制血糖,调脂,并平衡膳食,限制食盐摄入,限制饮酒,戒烟,适度减轻体重,坚持规律有氧运动,保持心理健康。对照组采用氨氯地平治疗,每天口服 5 mg,每天 1 次。治疗组在对照组基础上联合厄贝沙坦治疗, 口服 150 mg,每天 1 次。两组均持续治疗 8 周。

1.3 观察指标

(1)临床疗效[10]:于治疗结束时进行评价,DBP 降低超过 10 mmHg 或 SBP 降低超过 20 mmHg,或降低至正常范围,血糖指标达标为显效;DBP 降低再 10 mmHg, 或 SBP 降低为 10~20 mmHg,血糖指标正常为有效;未达到以上标准为无效。(2)于治疗前及治疗 4 周时采用水银柱式血压仪测定患者右臂坐位 SBP、DBP,连测 3 次(中间间隔 1 分钟),取平均值。(3)于治疗前及治疗后采集患者空腹外周静脉血,用全自动生化分析仪测定患者治疗前及治疗 4 周时空腹血糖 (Fasting plasma glucose,FPG)、糖化血红蛋白(glycosylated hemoglobin,Ghb)、总胆固醇(Total cholesterol,TC)、甘油三酯(Triglyceride,TG)。用化学发光免疫分析法测定治疗前后心肌肌钙蛋白 I (Cardiac troponin i,cTnI)、质量法测定肌酸激酶同工酶(creatine kinase-Isoenzyme,CK-MB)、酶联免疫吸附法测定乳酸脱氢酶(Lactate dehydrogenase,LDH)。(4)治疗期间不良反应的发生情况。

1.4 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用($\bar{x}\pm s$)表示,组间比较采用 t 检验,计数资料以[例(%)]表示,组间比较采用 x^2 检验或连续矫正比较,以 P<0.05 表示差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后,治疗组显效率为 67.35%,显著高于对照组(P<0.05),见表 1。

表 1 两组临床疗效的比较(例,%)

Table 1 Comparison of the clinical effects between the two groups (n,%)

Groups	n	Significantly effective	Effective	Ineffective	Significantly effective
Control group	49	22(44.90)	27(55.10)	0(0.00)	22(44.90)
Treatment group	49	33(67.35)	16(32.65)	0(0.00)	33(67.35)

2.2 两组治疗前后血压水平的比较

治疗后,两组 SBP、DBP 均较治疗前明显下降,且治疗组显著低于对照组(P<0.05),见表 2。

表 2 两组治疗前后血压水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the blood pressure between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	SBP(mmHg)	DBP(mmHg)
Control group	49	Before treatment	161.48± 7.89	98.49± 5.12
		After treatment	132.83± 3.61*	84.11± 2.63*
Treatment group	49	Before treatment	163.06± 7.13	99.26± 4.24
		After treatment	124.29± 3.38*#	79.54± 3.72*#

Note: vs. control group, #P<0.05; vs. Before treatment, *P<0.05.

2.3 两组治疗前后血糖水平的比较

治疗后,两组 FBG、HbA1c 均较治疗前明显下降,且治疗组显著低于对照组(P<0.05),见表 3。

2.4 两组治疗前后血脂水平的比较

治疗后,两组 TC、TG 均较治疗前明显下降,且治疗组显著低于对照组(P<0.05),见表 4。

表 3 两组治疗前后血糖水平的比较($\bar{x}\pm s$)

Table 3 Comparison of the blood glucose levels between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	Time	FPG(mmol/L)	Ghb(%)
Control group	49	Before treatment	7.65± 0.61	7.68± 0.58
		After treatment	5.79± 0.54*	5.90± 0.49*
Treatment group	49	Before treatment	7.44± 0.68	7.85± 0.63
		After treatment	5.18± 0.45*#	5.33± 0.41*#

Note: vs control group, #P<0.05;vs Before treatment, *P<0.05.

表 4 两组治疗前后血脂水平的比较($\bar{x}\pm s$)

Table 4 Comparison of the blood lipid levels between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	Time	TC(mmol/L)	TG(mmol/L)
Control group	49	Before treatment	6.55± 0.67	1.98± 0.23
		After treatment	5.46± 0.56*	1.76± 0.17*
Treatment group	49	Before treatment	6.73± 0.61	1.94± 0.25
		After treatment	4.27± 0.43*#	1.67± 0.13*#

Note: vs control group, #P<0.05;vs Before treatment, *P<0.05.

2.5 两组治疗前后心肌损伤指标的比较

治疗后，两组心肌损伤指标 cTnI、CK-MB 和 LDH 水平均较治疗前明显下降，且治疗组显著低于对照组(P<0.05)，见表5。

表 5 两组治疗前后心肌损伤指标比较($\bar{x}\pm s$)

Table 5 Comparison of the myocardial injury index between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	Time	cTnI(μg/L)	CK-MB(U/L)	LDH(U/L)
Control group	49	Before treatment	1.03± 0.06	18.19± 2.91	189.63± 20.18
		After treatment	0.53± 0.04*	16.14± 2.03*	163.27± 18.55*
Treatment group	49	Before treatment	1.05± 0.05	18.65± 2.49	181.41± 23.21
		After treatment	0.45± 0.02*#	14.48± 1.47*#	148.05± 14.29*#

Note: vs control group, #P<0.05;vs Before treatment, *P<0.05.

2.6 两组不良反应发生情况的比较

治疗过程中，两组不良反应总发生率比较无统计学差异(P>0.05)，见表 6。

表 6 两组不良反应的发生情况比较(例，%)

Table 6 Comparison of the incidence of adverse reaction between two groups (n, %)

Groups	n	Headache	Dizzy	Total incidence rate
Control group	49	1(2.04)	2(4.08)	3(6.12)
Treatment group	49	3(6.12)	4(8.16)	7(14.29)

3 讨论

糖尿病是危害老年人群健康的多发病及常见病，以高血糖为主要表现，且多合并程度不一的血脂代谢紊乱[11]。临床研究表明[12,13]糖尿病血糖控制不佳能够导致多个系统损伤，高血压为糖尿病最常见的伴发疾病，且流行病学研究显示[14]糖尿病为高血压的危险因素之一。高血压近年来已成为危害机体健康的公共卫生问题，糖尿病和高血压二者多相互影响，其共同发病的病情复杂，患者血压波动较大。临床研究建议[15]对于糖尿病伴高血压患者，在有效控制血糖的基础上应尽早给予抗高血压药物，以有助于保护靶器官。

机体钙摄取和血压有紧密关系，循环中钙离子能够影响细胞内钙浓度，导致心肌及血管平滑肌的收缩，从而影响血压。大部分高血压患者存在程度不一的钙代谢异常。研究表明[16,17]高血压患者尿钙排量较高，血钙含量则较低。钙通道阻滞剂为老年高血压的常用降压药，其中氨氯地平为长效钙拮抗剂，能够阻止钙离子内流，扩张外周小动脉，降低外周阻力，减少心肌耗能及氧需求，降低血压，减轻心脏后负荷[18,19]。氨氯地平的降压

作用较持久,能够将血压水平控制在理想范围内[20,21]。目前,单一用药的效果不甚理想,且疗程较长。本研究结果显示氨氯地平组治疗后有部分患者疗效判定为无效,提示其临床效果有待探究。

厄贝沙坦为血管紧张素转换酶抑制剂,能够拮抗血管紧张素Ⅰ表达,产生降压效应。临床研究显示厄贝沙坦能够通过提高胰岛素敏感性、减少胰岛素信号通路受损等途径干预机体糖代谢,起到降血糖作用[22]。此外[23],厄贝沙坦能够改善肾脏血流动力学,减少尿蛋白,降低肾小球跨膜压力和肾血管阻力,增加肾脏血流量,逆转肾器官受损。Haneef J 等研究发现[24]厄贝沙坦能够通过减少缓激肽的降解,降低外周阻力,从而减轻心脏前后负荷,增加机体的心输出量。相关研究报道[25]钙通道阻滞剂联合血管紧张素转换酶抑制剂有协同降压作用。本研究结果显示氨氯地平联合厄贝沙坦治疗后显效率较高,且两组治疗后血压及血糖指标均较治疗前下降,但氨氯地平联合厄贝沙坦组明显低于氨氯地平组,提示二者联合更能有效调节患者糖代谢,鉴于其与氨氯地平存在作用持续时间长的特点,加之厄贝沙坦有辅助降压作用,其双重作用可有效控制患者血压,减少糖代谢紊乱风险。糖尿病伴高血压患者多存在一定程度的糖脂质代谢紊乱,致患者血 TC、TG 浓度明显上升,从而能够促进血管内皮功能失调,导致血压上升,形成恶性循环[26-28]。本研究结果显示患者治疗前 TC、TG 水平相对较高,证实糖尿病伴高血压患者可能存在血脂代谢异常,两组治疗后其 TC、TG 水平均较治疗前下降,氨氯地平联合厄贝沙坦组 TG、TC 水平明显低于氨氯地平组,提示两者联合对老年糖尿病伴高血压患者血脂代谢调节有一定优势,可确切提高临床效果。

研究表明,长期血压过高能够对动脉内膜产生影响,促进斑块形成,增大外周血管阻力[29]。Mattioli AV 等[30]研究显示老年人群心脏结构容易发生顺应性下降、致室壁增厚等心脏结构改变,增加心脏负荷,易导致心肌缺血。已知 cTnI 仅在心室肌及心房肌中分布,其有独特的基因序列,机体正常状态下 cTnI 的含量较低,为心肌特异的心肌蛋白,也是心肌损伤及心脏不良事件的敏感标志物,其可客观反映心肌损伤[31,32]。心肌细胞膜完整的状态下其无法通过细胞膜达到血液循环,心肌缺血 - 再灌注损伤时能够刺激 cTnI 表达。Joob B 等[33]研究表明冠心病患者经皮介入术治疗后其血液中 cTnI 水平有所增加,提示 cTnI 能够反映围术期心肌损伤情况。CK-MB 为心肌组织受损的另一敏感指标之一,心肌细胞受损时 CK-MB 可释放至血液中,导致 CK-MB 上升,CK-MB 在心肌细胞中的含量最高,因此对心肌损伤的诊断有较高的特异性[34,35]。LDH 不仅在心肌内分布,也存在于骨骼肌、肝脏等中,心肌受损时 LDH 上升,但其降低较缓慢。本研究结果显示治疗后患者 cTnI、CK-MB、LDH 水平较治疗前下降,且氨氯地平联合厄贝沙坦组降低更明显,表明二者联合用药能够改善糖尿病伴高血压患者心肌状态,有助于缓解预防心血管疾病的恶化,分析原因可能与联合用药的降压效果确切稳定,可减轻血压对心血管形成的影响,厄贝沙坦还可延缓、逆转心室重构,进一步抑制心肌肥厚,改善机体心血管及血管内皮功能,提高血管及心肌的顺应性,从而更有利于心功能的改善。此外,两组用药期间仅少数患者发生轻微不良反应,提示联合用药的安全性较高。

综上所述,氨氯地平联合厄贝沙坦能够提高老年糖尿病伴高血压的临床治疗效果,改善糖脂质代谢及减轻心肌损伤。但本研究存在样本量偏小、随访时间较短等不足,其研究结论需进一步大样本的临床研究证实。

参 考 文 献(References)

[1] Tatsumi Y, Ohkubo T. Hypertension with diabetes mellitus: significance from an epidemiological perspective for Japanese[J]. Hypertens Res, 2017, 40(9): 795-806

[2] Cryer MJ, Horani T, DiPette DJ. Diabetes and Hypertension: A Comparative Review of Current Guidelines [J]. J Clin Hypertens (Greenwich), 2016, 18(2): 95-100

[3] Gupta R, Sharma KK, Lodha S, et al. Quality of Hypertension Management in Type 2 Diabetes in India: A Multisite Prescription Audit [J]. J Assoc Physicians India, 2018, 66(9): 20-25

[4] Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms[J]. Can J Cardiol, 2018, 34(5): 575-584

[5] Lee JY, Ryu S, Sung KC. Association of baseline level of physical activity and its temporal changes with incident hypertension and diabetes mellitus[J]. Eur J Prev Cardiol, 2018, 25(10): 1065-1073

[6] Borghi C, Urso R, Cicero AF. he cost-effectiveness of irbesartan for hypertension [J]. Expert Rev Pharmacoecon Outcomes Res, 2015, 15 (2): 199-207

[7] Gottwald-Hostalek U, Sun N, Barho C, et al. Management of Hypertension With a Fixed-Dose (Single-Pill) Combination of Bisoprolol and Amlodipine[J]. Clin Pharmacol Drug Dev, 2017, 6(1): 9-18

[8] Nemtsova V, Bilovol O, Vysotska O, et al. influence of lipid metabolism control on the telomeres relative length in patients with isolated hypertension and in combination with diabetes mellitus type 2 [J]. Georgian Med News, 2019, 11(291): 58-63

[9] Morris-Paxton AA, Rheeder P, Ewing RG, et al. Detection, referral and control of diabetes and hypertension in the rural Eastern Cape Province of South Africa by community health outreach workers in the rural primary healthcare project: Health in Every Hut [J]. Afr J Prim Health Care Fam Med, 2018, 10(1): e1-e8

[10] Muntner P,Whelton PK,Woodward M, et al. A Comparison of the 2017 American College of Cardiology/American Heart Association Blood Pressure Guideline and the 2017 American Diabetes Association Diabetes and Hypertension Position Statement for U.S. Adults With Diabetes[J]. Diabetes Care, 2018, 41(11): 2322-2329

[11] Libianto R, Batu D, MacIsaac RJ, et al. Pathophysiological Links Between Diabetes and Blood Pressure [J]. Can J Cardiol, 2018, 34(5): 585-594

[12] Tilov B, Semerdzhieva M, Bakova D, et al. Study of the relationship between aggression and chronic diseases (diabetes and hypertension) [J]. J Eval Clin Pract, 2016, 22(3): 421-424

[13] Chahoud J, Mrad J, Semaan A, et al. Prevalence of diabetes mellitus among patients with essential arterial hypertension [J]. J Med Liban, 2015, 63(2): 74-80

[14] Pedro JM, Brito M, Barros H. Prevalence, awareness, treatment and control of hypertension, diabetes and hypercholesterolaemia among adults in Dande municipality, Angola [J]. Cardiovasc J Afr, 2018, 29 (2): 73-81

[15] Papadopoulou E, Angeloudi E, Karras S, et al. The optimal blood pressure target in diabetes mellitus: a quest coming to an end [J]. J Hum Hypertens, 2018, 32(10): 641-650

[16] Sethi BK, Baruah MP, Kumar AS. Blood Pressure Variability in Patients with Diabetes Mellitus with Hypertension: Treatment Recommendations and Role of Amlodipine [J]. J Assoc Physicians India, 2017, 65(3): 67-71

[17] Fleig SV, Weger B, Haller H, et al. Effectiveness of a Fixed-Dose, Single-Pill Combination of Perindopril and Amlodip ine in Patients with Hypertension: A Non-Interventional Study [J]. Adv Ther, 2018, 35(3): 353-366

[18] Podzolkov VI, Bragina AE, Osadchiy KK. A fixed-dose lisinopril+amlodipine+rosuvastatin combination: prospects for its use in patients with hypertension and concomitant dyslipidemia [J]. Ter Arkh,2017, 89(12): 133-140

[19] Şen S, Demir M, Yiğit Z, et al. Efficacy and Safety of S-Amlodipine 2.5 and 5 mg/d in Hypertensive Patients Who Were Treatment-Naive or Previously Received Antihypertensive Monotherapy [J]. J Cardiovasc Pharmacol Ther, 2018, 23(4): 318-328

[20] Simonyi G, Ferenci T. One year adherence of ramipril versus ramipril/amlodipine fixed dose combination therapy in hypertension [J]. Orv Hetil, 2017, 158(42): 1669-1673

[21] Slíva J. Current position of a fixed combination telmisartan with amlodipine in treatment of essential arterial hypertension [J]. Vnitr Lek, 2016, 62(9): 699-702

[22] Byrd JB, Chertow GM, Bhalla V. Hypertension Hot Potato - Anatomy of the Angiotensin-Receptor Blocker Recalls [J]. N Engl J Med, 2019, 380(17): 1589-1591

[23] Hu S, Cheng J, Weinstock J, et al. A gender-specific association of the polymorphism Ile197Met in the kininogen 1 gene with plasma irbesartan concentrations in Chinese patients with essential hypertension[J]. J Hum Hypertens, 2018, 32(11): 781-788

[24] Haneef J, Chadha R. Antioxidant-Based Eutectics of Irbesartan: Viable Multicomponent Forms for the Management of Hypertension[J]. AAPS PharmSciTech, 2018, 19(3): 1191-1204

[25] Omboni S, Malacco E, Napoli C, et al. Efficacy of Zofenopril vs. Irbesartan in Combination with a Thiazide Diuretic in Hypertensive Patients with Multiple Risk Factors not Controlled by a Previous Monotherapy: A Review of the Double-Blind, Randomized "Z" Studies[J]. Adv Ther, 2017, 34(4): 784-798

[26] Shiga T. Cardiac Troponin as a Specific and Non-Specific Biomarker for CardiovascularEvents[J]. Int Heart J, 2016, 57(3): 265-267

[27] Grenier J, Goodman SG, Leiter LA, et al. Blood Pressure Management in Adults With Type 2 Diabetes: Insights From the Diabetes Mellitus Status in Canada (DM-SCAN) Survey [J]. Can J Diabetes, 2018, 42(2): 130-137

[28] Guclu A, Erdur FM, Turkmen K. The Emerging Role of Sirtuin 1 in Cellular Metabolism, Diabetes Mellitus, Diabetic Kidney Disease and Hypertension [J]. Exp Clin Endocrinol Diabetes, 2016, 124 (3): 131-139

[29] Spallone V. Update on the Impact, Diagnosis and Management of Cardiovascular Autonomic Neuropathy in Diabetes: What Is Defined, What Is New, and What Is Unmet [J]. Diabetes Metab J, 2019, 43(1): 3-30

[30] Mattioli AV, Sciomer S, Moscucci F, et al. Cardiovascular prevention in women: a narrative review from the Italian Society of Cardiology working groups on 'Cardiovascular Prevention, Hypertensionand peripheral circulation' and on 'Women Disease' [J]. J Cardiovasc Med (Hagerstown), 2019, 20(9): 575-583

[31] Nikolov A, Tzekova M, Blazhev A. Relationship between Lipid Indices, Type IV Collagen Turnover and the Development of Microvascular Complications in Diabetic Patients with Arterial Hypertension [J]. Folia Med (Plovdiv), 2019, 61(2): 231-239

[32] Metskas LA, Rhoades E. Order-Disorder Transitions in the Cardiac Troponin Complex[J]. J Mol Biol, 2016, 428(15): 2965-77

[33] Joob B, Wiwanitkit V. Hepatitis B carrier on cardiac troponin I [J]. J Chin Med Assoc, 2017, 80(9): 608

[34] Domanski M, Farkouh ME, Zak V, et al. Relation of Post-Coronary Artery Bypass Graft Creatine Kinase-MB Elevations and New Q Waves With Long-Term Cardiovascular Death in Patients With Diabetes Mellitus and Multivessel Coronary Artery Disease[J]. Am J Cardiol, 2016, 118(11): 1655-1660

[35] Quiroga B, Vega A, Abad S, et al. Creatine-kinase and dialysis patients, a helpful tool for stratifying cardiovascular risk[J]. Nefrologia, 2016, 36(1): 51-56

(上接第 3395 页)

[20] Jonker F H, Hagemans J, Verhoef C, et al. The impact of hospital volume on perioperative outcomes of rectal cancer [J]. European Journal of Surgical Oncology the Journal of the European Society of Surgical Oncology & the British Association of Surgical Oncology, 2017, 43 (10): 1894

[21] GevaR, Davidovics H, Soyfer S, et al. Does residual microscopic disease after chemoradiotherapy for locally advanced rectal cancer translate into a good clinical outcome?[J]. Colorectal Disease, 2017, 19(3): 237-242

[22] Georgiou C L, Pezaro C, Sengupta S. Putting guidelines into practice: has the era of perioperative chemotherapy arrived?[J]. Translational Andrology & Urology, 2018, 7(S2): S255-S257

[23] Vychnevskaia K, Dumont F, Agostini J, et al. Prognostic Value of Sterilized Lymph Nodes After Preoperative Chemoradiotherapy for Patients with ypN0 Rectal Cancer [J]. Annals of Surgical Oncology, 2017, 24(5): 1304-1311

[24] Han J, Zhang X, Zhang A D, et al. Impact of primary tumor site on the prognosis in different stage colorectal cancer patients after radical resection[J]. Zhonghua Wai Ke Za Zhi, 2018, 56(1): 68-73

[25] Wu A, Wang L, Du C, et al. Outcome of watch and wait strategy or organ preservation for rectal cancer following neoadjuvant chemoradiotherapy: report of 35 cases from a single cancer center[J]. Chinese journal of gastrointestinal surgery, 2017, 20(4): 417-424

[26] M. A. Pereira, A. R. Dias, S. F. Faraj, et al. Erratum to: One-level step section histological analysis is insufficient to confirm complete pathological response after neoadjuvant chemoradiation for rectal cancer [J]. Techniques in coloproctology, 2017, 21(9): 745-754