接受肾上腺切除术或螺内酯治疗的原发性醛固酮增多症患者代谢转归[*]

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【摘要】 目的　探讨原发性醛固酮增多症（原醛症）患者经肾上腺切除手术（ADX）或螺内酯治疗后的代谢转归及其影响因素。 方法　回顾性分析2018年3月−2020年10月经四川大学华西医院内分泌科确诊的70例醛固酮瘤（APA）和86例特发性醛固酮增多症（IHA）患者的临床资料，APA组患者均进行ADX治疗，IHA患者均服用盐皮质激素受体拮抗剂（螺内酯）治疗，分析患者治疗后代谢指标的转归情况及组间差异。 结果　APA组与IHA组患者治疗前年龄、性别、高血压病程、最高血压、最低血压、体质量指数（BMI）、血脂、空腹血糖、肾功能差异无统计学意义，IHA组患者的腰围、血钾水平和血浆肾素活性高于APA组（P均<0.05）。治疗后所有患者的血压、血钾及血浆醛固酮浓度显著改善，出现三酰甘油升高伴肾功能恶化（$P \leqslant 0.001$）。多因素回归显示三酰甘油水平与IHA组患者经螺内酯治疗、治疗后BMI及肌酐水平有关。APA组患者经肾上腺切除后空腹血糖改善（$P=0.041$），但IHA组患者经螺内酯治疗后空腹血糖升高（$P=0.037$）。 结论　原醛症患者治疗后可能仍然存在糖脂代谢异常及肾功能恶化，螺内酯治疗可能有更差的代谢结局。

【关键词】 原发性醛固酮增多症　　治疗方式　　代谢转归

Metabolic Outcomes of Primary Aldosteronism Patients Receiving Adrenalectomy or Spironolactone Treatments
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【Abstract】 **Objective**　To investigate the metabolic outcomes of primary aldosteronism (PA) patients receiving adrenalectomy (ADX) or spironolactone treatment and the contributing factors to the metabolic outcomes. **Methods**　The clinical data of 70 patients with aldosterone-producing adenoma (APA) and 86 patients with idiopathic hyperaldosteronism (IHA) were retrospectively analyzed. All subjects received confirmatory diagnosis of APA or IHA at the Department of Endocrinology and Metabolism, West China Hospital between March 2018 and October 2020. APA patients underwent ADX, while IHA patients were given spironolactone, a mineralocorticoid receptor antagonist (MRA). After ADX or spironolactone treatment, the outcomes of the metabolic indicators and the inter-group differences between the APA patients and IHA patients were studied. **Results**　There was no significant difference between the baseline data of the APA group and those of the IHA group in terms of age, sex, duration of hypertension, maximum systolic blood pressure (SBP-max), maximum diastolic blood pressure (DBP-max), body mass index (BMI), fasting blood glucose (FBG), lipid parameters, and renal function. IHA patients had higher waist circumference, serum potassium, and plasma renin activity (PRA) than those of the APA patients (all $P<0.05$). All patients showed significant improvement in blood pressure, blood potassium, and plasma aldosterone at follow-up. However, they also showed increased triglycerides (TG) accompanied by deterioration in renal function ($P \leqslant 0.001$). Multiple regression showed that TG levels were associated with spironolactone treatment for IHA patients and post-treatment BMI and creatinine levels. Furthermore, APA patients showed improvement in their FBG after ADX ($P=0.041$), while IHA patients showed elevated levels of FBG after spironolactone treatment ($P=0.037$). **Conclusion**　After treatment, PA patients still may experience abnormal lipid metabolism and deteriorating renal function. Spironolactone therapy may give rise to worse glucolipid metabolism than ADX therapy does.

原发性醛固酮增多症(primary aldosteronism, PA, 简称原醛症)是最常见的继发性高血压, 在我国新诊断高血压人群中的患病率超过4%[1], 其发生机制为肾上腺皮质增生或腺瘤导致醛固酮自主高分泌, 相较于原发性高血压患者有更严重的心脑肾损害[2], 也更容易合并代谢紊乱[3]。已有研究发现原醛症患者的代谢异常(如糖尿病)在其心脑血管疾病发生中具有重要作用。既往关于原醛症患者治疗后的研究大多关注血压、血钾和激素的缓解情况[4-5], 而对于患者治疗后的代谢转归关注较少, 尤其是醛固酮瘤(aldosterone-producing adenoma, APA)和特发性醛固酮增多症(idiopathic hyperaldosteronism, IHA)患者经治疗后的代谢差异及潜在影响因素尚无定论。少数研究发现肾上腺切除(adrenalectomy, ADX)后原醛症患者胰岛素敏感性显著改善, 而盐皮质激素受体拮抗剂(mineralocorticoid receptor antagonists, MRA)治疗后则改善不明显[6], 也有研究者发现原醛症患者经ADX或MRA治疗后胰岛素敏感性反而下降[7]。BOCHUD等[8]研究提示原醛症患者血脂水平与血浆醛固酮浓度(plasma aldosterone concentration, PAC)相关, ADX治疗导致新发或者持续性脂代谢异常风险[9], 但影响治疗后糖脂代谢的因素尚未明确。基于此, 本研究分析了原醛症患者经ADX或螺内酯治疗后的糖脂代谢改变及可能影响因素, 以期更好地实施原醛症的长期规范化治疗。

1　对象与方法

1.1　研究对象

四川大学华西医院在2018年3月–2020年10月期间收治的符合诊断标准的原醛症患者156例, 根据分型诊断分为APA组70例和IHA组86例。研究中的APA组患者均进行ADX治疗, IHA患者均服用螺内酯治疗。本研究项目经四川大学华西医院伦理委员会审核批准(2019年审692号)。

1.2　纳入及排除标准

原醛症的诊断依据2016年美国内分泌协会指南及我国共识标准。纳入患者在筛查前均停服影响醛固酮肾素比值(aldosterone renin ratio, ARR)的药物, 并尽量纠正低血钾, ARR筛查阳性的患者进一步行卡托普利抑制试验和/或盐水负荷试验。排除标准: ①严重肝、肾功能不全及严重心脏病患者; ②备孕、妊娠期或哺乳期妇女; ③依从性差, 治疗后不能按照要求进行随访、复查者。分型诊断标准依据肾上腺静脉采血(adrenal venous sampling, AVS)、术后病理及治疗后临床缓解情况。

1.3　研究方法

收集研究对象确诊时的年龄、性别、腰围、体质量指数(BMI)、最高血压值(SBP-max和DBP-max)、高血压病程、最低血钾(K-min)、空腹血糖(fasting blood-glucose, FBG)、糖耐量试验(oral glucose tolerance test, OGTT)、三酰甘油(triglycerides, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、血肌酐、尿酸、估算肾小球滤过率(estimated glomerular filtration rate, e-GFR)水平、立位血浆肾素活性(plasma renin activity, PRA)、立位PAC; 以及治疗后的降压药物使用情况、血压、BMI、腰围、血钾、FBG、血脂、肾功能、PRA及PAC。

1.4　统计学方法

连续变量若满足正态分布, 使用两独立样本t检验和配对样本t检验, 以$\bar{x} \pm s$表示; 若不满足正态分布, 使用Mann-Whitney U检验和配对样本Wilcoxon检验, 以中位数(P_{25}, P_{75})表示。分类变量使用卡方检验, 以频数和百分率表示。将单因素分析中$P < 0.1$和临床上认为有意义的变量纳入多因素回归分析。用Excel软件整理原始资料, R 4.2.2统计学软件分析数据。$P < 0.05$为差异有统计学意义。

2　结果

2.1　治疗前APA与IHA组间比较

两组患者的年龄、性别、高血压病程、SBP-max、DBP-max、FBG、BMI及血脂参数差异均无统计学意义。IHA组患者腰围大于APA组($P = 0.023$)。APA组血肌酐、尿酸水平稍低, e-GFR水平更高, 但差异无统计学意义。治疗前, APA患者低钾血症发生率、ARR值高于IHA组, 血钾、既往最低血钾及PRA水平低于IHA组(P均<0.05)。见表1。

2.2　治疗后患者生化及代谢转归

本组患者在治疗后平均8个月时接受随访, 所有患者PRA恢复正常, 低钾血症明显缓解, PAC较治疗前明显下降。

APA患者经ADX治疗后, FBG水平较治疗前下降($P = 0.041$), 血脂未见明显变化($P > 0.05$)。IHA患者经螺内酯治疗后, FBG和TG水平升高(P均<0.05)。同时, 治疗后两组患者肾功能均出现下降, e-GFR平均下降幅度超过13 mL/(min·1.73 m²), 血肌酐、尿素及尿酸水平也上升(P均≤0.001)。见表2。

表 1　治疗前APA与IHA组间临床指标比较

Table 1　Baseline data of patients with APA and IHA

Variable	APA group (n= 70)	IHA group (n= 86)	$t/z/\chi^2$	P
Age/yr.	48.9±12.1	49.9±9.1	t=0.610	0.543
Women/case (%)	42 (60)	53 (62)	χ^2=0.002	0.966
Duration of hypertension/month, median (P_{25}, P_{75})	60 (11, 120)	72 (12, 128)	z=0.940	0.348
SBP-max/mmHg, median (P_{25}, P_{75})	180 (160, 190)	170 (160, 187)	z=−1.179	0.239
DBP-max/mmHg, median (P_{25}, P_{75})	110 (100, 110)	104 (100, 110)	z=−1.508	0.132
Waist circumference/cm, median (P_{25}, P_{75})	84.6 (83.7, 87.8)	88.1 (82.1, 91.0)	z=2.268	0.023
BMI/(kg/m²)	24.3±3.8	24.5±3.5	t=0.287	0.775
Glycemic abnormalities/case (%)[a]			χ^2=2.755	0.252
Prediabetes	3 (4)	9 (10)		
Diabetes	13 (19)	11 (13)		
Hypokalemia/case (%)	59 (84)	58 (67)	χ^2=4.975	0.026
FBG/(mmol/L), median (P_{25}, P_{75})	5 (4.63, 5.52)	4.96 (4.58, 5.34)	z=−0.549	0.584
Urea/(mmol/L), median (P_{25}, P_{75})	4.4 (3.8, 5.6)	4.5 (3.7, 5.2)	z=−0.715	0.476
Creatinine/(μmol/L), median (P_{25}, P_{75})	63.35 (53.0, 75.8)	65.5 (58.3, 77.8)	z=1.246	0.213
e-GFR/(mL/[min·1.73 m²]), median (P_{25}, P_{75})	103.0 (91.3, 111.0)	98.8 (93.1, 106.2)	z=−1.351	0.177
Renal insufficiency/case (%)[b]	17 (24)	16 (19)	χ^2=0.445	0.505
Uric acids/(μmol/L)	299.9±81.5	323.4±85.2	t=1.753	0.082
TG/(mmol/L), median (P_{25}, P_{75})	1.21 (0.80, 1.70)	1.23 (0.90, 1.76)	z=0.539	0.590
TC/(mmol/L)	4.3±0.8	4.4±0.8	t=0.726	0.469
HDL-C/(mmol/L), median (P_{25}, P_{75})	1.32 (1.12, 1.55)	1.27 (1.03, 1.48)	z=−1.563	0.119
LDL-C/(mmol/L)	2.5±0.7	2.6±0.7	t=1.303	0.195
Dyslipidemia/case (%)	8 (11)	15 (17)	χ^2=0.683	0.408
K/(mmol/L)	3.4±0.5	3.6±0.4	t=2.057	0.041
K-min/(mmol/L), median (P_{25}, P_{75})	2.96 (2.47, 3.28)	3.3 (2.68, 3.59)	z=2.375	0.018
PRA/(ng/[mL·h]), median (P_{25}, P_{75})	0.15 (0.07, 0.41)	0.25 (0.12, 0.63)	z=2.146	0.032
PAC/(ng/dL), median (P_{25}, P_{75})	28.4 (20.7, 39.4)	25.1 (18.8, 36.1)	z=−1.395	0.164
ARR/(ng/dL：ng/[mL·h]), median (P_{25}, P_{75})	134.4 (63.0, 481.6)	76.2 (46.3, 243.3)	z=−2.199	0.028

BMI: body mass index; FBG: fasting blood-glucose; e-GFR: estimated glomerular filtration rate; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; K-min: minimum blood potassium; PRA: plasma renin activity; PAC: plasma aldosterone; ARR: aldosterone renin ratio. a, Glycemic abnormalities: prediabetes (fasting plasma glucose levels 6.1-6.9 mmol/L or 2 h serum glucose levels 7.8-11.0 mmol/L); diabetes (fasting plasma glucose levels ≥7.0 mmol/L or 2 h serum glucose levels ≥11.1 mmol/L).　b, Renal insufficiency: estimated glomerular filtration rate<90 mL/(min·1.73 m²). 1 mmHg=0.133 kPa.

表 2　APA组与IHA组治疗前后指标比较

Table 2　Baseline and follow-up data of patients with APA and IHA

Variable	APA group (n=70)				IHA group (n=86)			
	Before treatment	After treatment	t	P	Before treatment	After treatment	t	P
Waist circumference/cm	85.3±7.3	87.9±9.9	2.917	0.005	86.9±7.5	87.9±6.6	−0.258	0.798
BMI/(kg/m²)	24.3±3.8	24.8±3.2	0.926	0.448	24.5±3.5	25.2±2.5	0.507	0.615
FBG/(mmol/L)	5.14±0.74	4.96±0.46	−2.079	0.041	5.08±0.66	5.24±0.43	2.119	0.037
Urea/(mmol/L)	4.69±1.42	5.44±1.65	3.15	0.002	4.48±1.22	5.58±1.50	5.597	0.001
Creatinine/(μmol/L)	65.3±16.5	80.6±20.2	8.302	<0.001	68.5±15.2	78.9±16.8	7.327	0.001
e-GFR/(mL/[min·1.73 m²])	101.0±15.8	87.6±19.3	−7.031	<0.001	98.6±12.4	86.9±14.9	−8.310	0.001
Uric acids/(μmol/L)	300.0±81.5	346.0±79.0	4.489	<0.001	323.0±85.2	363.0±85.4	4.584	0.001
TG/(mmol/L)	1.34±0.66	1.36±0.54	0.201	0.883	1.39±0.66	1.55±0.45	2.184	0.031
TC/(mmol/L)	4.30±0.78	4.25±0.80	−0.492	0.624	4.40±0.85	4.44±0.86	0.373	0.710
HDL-C/(mmol/L)	1.36±0.33	1.42±0.43	1.13	0.262	1.28±0.34	1.26±0.35	−0.697	0.488
LDL-C/(mmol/L)	2.48±0.67	2.48±0.65	−0.019	0.985	2.63±0.74	2.53±0.64	−1.083	0.282
K/(mmol/L)	3.41±0.50	4.19±0.42	9.863	<0.001	3.58±0.45	4.23±0.38	10.118	0.001
PRA/(ng/[mL·h])	0.32±0.33	3.40±2.75	9.46	<0.001	0.38±0.33	2.71±2.65	8.200	0.001
PAC/(ng/dL)	31.1±13.5	18.0±9.5	−6.033	<0.001	28.9±13.6	20.2±11.2	−4.666	0.001
ARR/(ng/dL：ng/[mL·h])	270.0±252.0	11.7±13.3	−8.569	<0.001	179.0±193.0	16.0±14.6	−7.800	0.001

The abbreviations are explained in the note to Table 1.

经ADX和螺内酯治疗后的两组患者血压、血钾、PRA及PAC水平均差异无统计学意义，但FBG、TG及HDL-C水平差异有统计学意义，螺内酯治疗后FBG、TG水平更高，HDL-C水平更低(P均<0.05)。见表3。

多因素回归分析显示治疗后FBG水平与ADX治疗负相关〔β= -0.228, 95%置信区间(confidence interval, *CI*)：-0.426 ~ -0.030, P= 0.024〕，与治疗后BMI水平(β= 0.031, 95%*CI*: 0.002 ~ 0.059, P= 0.032)正相关，见表4。治疗后TG水平除了与ADX治疗呈负相关、BMI正相关外，还与治疗后血肌酐水平存在正向关联(β= 0.010, 95%*CI*:

0.002 ~ 0.018, P= 0.021)，见表5。治疗后e-GFR水平与患者年龄及治疗后血钾呈负相关，而与K-min及基础eGFR正相关，见表6。

3 讨论

已有研究表明原醛症患者更易合并代谢综合征如糖脂代谢异常等[10-11]，可能加重心脑血管及肾脏不良预后。因此，经ADX或MRA治疗后能否达到理想的糖脂代谢转归，可能是影响患者远期并发症的关键因素。

本研究证实原醛症患者(无论APA还是IHA)均存在

表3 APA组和IHA组治疗后指标比较
Table 3 Follow-up data of patients receiving ADX or spironolactone treatment

Variable	APA group (*n*=70)	IHA group (*n*=86)	$t/z/\chi^2$	*P*
BMI/(kg/m²)*	24.8±3.2	25.2±2.5	t=0.793	0.430
Waist circumference/cm*	87.9±9.9	87.6±6.6	t=-0.206	0.838
SBP/mmHg, median (P_{25}, P_{75})	130 (120, 141)	130 (120, 137)	z=0.223	0.825
DBP/mmHg, median (P_{25}, P_{75})	88 (81, 93)	87 (80, 90)	z=-1.079	0.281
Blood pressure remission/case (%)ᵃ	28 (40)	27 (31)	χ^2=0.903	0.342
MRA/case (%)	14 (20)	86 (100)	χ^2=103.880	<0.001
K/(mmol/L), median (P_{25}, P_{75})	4.1 (4.0, 4.4)	4.2 (4.0, 4.5)	z=1.144	0.253
Hypokalemia/case (%)	7 (10)	7 (8)	χ^2=0.015	0.902
FBG/(mmol/L), median (P_{25}, P_{75})	5.0 (4.7, 5.1)	5.2 (4.9, 5.4)	z=3.827	<0.001
Abnormal glucose metabolism/case (%)	13 (19)	16 (19)	χ^2=0.001	1
Dyslipidemia/case (%)	10 (14)	21 (24)	χ^2=1.893	0.169
TG/(mmol/L), median (P_{25}, P_{75})	1.3 (1.1, 1.5)	1.5 (1.1, 1.8)	z=2.038	0.042
TC/(mmol/L), median (P_{25}, P_{75})	4.1 (3.8, 4.8)	4.3 (4.0, 5.0)	z=1.389	0.165
HDL-C/(mmol/L), median (P_{25}, P_{75})	1.3 (1.1, 1.6)	1.2 (1.0, 1.4)	z=-2.268	0.023
LDL-C/(mmol/L), median (P_{25}, P_{75})	2.5 (2.3, 2.9)	2.47 (2.1, 3.0)	z=0.457	0.649
Urea/(mmol/L), median (P_{25}, P_{75})	5.3 (4.7, 6.1)	5.3 (4.8, 6.1)	z=0.383	0.703
Creatinine/(μmol/L), median (P_{25}, P_{75})	81.2 (67.0, 92.8)	74.7 (68.0, 87.0)	z=-0.941	0.347
e-GFR/(mL/[min·1.73 m²]), median (P_{25}, P_{75})	88.5 (76.1, 98.0)	90.1 (78.7, 95.9)	z=0.160	0.874
Uric acids/(μmol/L), median (P_{25}, P_{75})	341.6 (301.0, 381.3)	354.8 (301.0, 418.3)	z=0.765	0.446
Renal insufficiency/case (%)	43 (61)	43 (50)	χ^2=1.602	0.206
PRA/(ng/[mL·h]), median (P_{25}, P_{75})	2.7 (1.1, 4.8)	1.76 (1.0, 3.1)	z=-1.781	0.075
PAC/(ng/dL), median (P_{25}, P_{75})	14.8 (11.0, 22.9)	18.9 (10.8, 26.3)	z=1.174	0.241
ARR/(ng/dL：ng/[mL·h]), median (P_{25}, P_{75})	6.2 (3.5, 13.8)	10.0 (3.6, 24.0)	z=1.886	0.059

* APA group *n*=45, IHA group *n*=56. The abbreviations are explained in the note to Table 1. MRA: mineralocorticoid receptor antagonists. a, Blood pressure remission: no antihypertensive drugs were used within 3 months at follow-up and blood pressure was measured according to standard and multiple (≥3 times) measurements, with systolic blood pressure<140 mmHg and diastolic blood pressure<90 mmHg. 1 mmHg=0.133 kPa.

表4 影响治疗后FBG水平的多因素回归
Table 4 Multivariate linear regression of variables associated with post-treatment FBG

Variable	Standard β	β (95% *CI*)	VIF	*P*
Age	0.060	0.002 (-0.007, -0.012)	1.87	0.630
ADX	-0.258	-0.228 (-0.426, -0.030)	1.55	0.024
Potassium before treatment	0.062	0.057 (-0.134, 0.248)	1.40	0.559
Log (PAC before treatment)	-0.154	-0.186 (-0.420, 0.047)	1.16	0.116
e-GFR before treatment	-0.119	-0.004 (-0.012, 0.004)	1.89	0.339
BMI after treatment	0.204	0.031 (0.002, 0.059)	1.07	0.032
Log (PAC after treatment)	0.078	0.074 (-0.118, 0.267)	1.29	0.445

Adjusted R^2=0.210, P<0.001. β: coefficient; *CI*: confidence interval; VIF: variance inflation factor; ADX: adrenalectomy. The abbreviations are explained in the note to Table 1.

表 5　影响治疗后TG水平的多因素回归
Table 5　Multivariate linear regression of variables associated with post-treatment TG

Variable	Standard β	β (95% CI)	VIF	P
Male	0.156	0.076 (−0.141, 0.292)	1.49	0.489
Treat with ADX	−0.481	−0.233 (−0.421, −0.046)	1.21	0.015
e-GFR before treatment	−0.092	−0.003 (−0.010, 0.004)	1.34	0.371
BMI after treatment	0.248	0.042 (0.009, 0.074)	1.20	0.012
Creatinine after treatment	0.248	0.010 (0.002, 0.018)	2.94	0.021
Uric acids after treatment	−0.046	−0.001 (−0.002, 0.001)	2.17	0.726

Adjusted R^2=0.257, P<0.001. The abbreviations are explained in the note to Tables 1 and 4.

表 6　影响治疗后e-GFR水平的多因素回归
Table 6　Multivariate linear regression of variables associated with post-treatment e-GFR

Variable	Standard β	β (95% CI)	VIF	P
Age	−0.248	−0.383 (−0.685, −0.082)	1.87	0.013
SBP	−0.086	−0.100 (−0.271, 0.070)	1.05	0.246
K-min	0.152	4.369 (0.154, 8.585)	1.06	0.042
Potassium after treatment	−0.228	−9.701 (−15.96, −3.440)	1.06	0.003
TG	−0.122	−3.859 (−8.583, 0.865)	1.08	0.108
Log (PAC after treatment)	0.254	9.326 (3.886, 14.766)	1.28	0.001
e-GFR before treatment	0.339	0.424 (0.169, 0.679))	2.05	0.001

Adjusted R^2=0.257, P<0.001. The abbreviations are explained in the note to Tables 1 and 4.

一定程度的糖脂代谢异常。APA患者经单侧肾上腺切除治疗后FBG明显降低, 但IHA患者经螺内酯治疗后FBG升高, 多因素回归显示ADX治疗、较低的BMI与FBG下降相关, 提示ADX治疗较螺内酯治疗可能对血糖控制更为有益。既往有研究发现经过平均5.2年随访时间, 手术治疗后的患者新发糖尿病风险降低, 而MRA治疗后患者上述风险反而增加[12]。

少数其他研究也观察到了同样的情况。TAIPAI团队发现原醛症患者治疗后HOMA-IR与PAC水平存在非线性正相关, 螺内酯治疗后PAC明显升高, 其PAC>30 ng/dL及HOMA-IR>2风险明显高于手术治疗患者, 该研究还提出治疗后PAC<30 ng/dL可能有助于改善胰岛素敏感性[13], 由此推测螺内酯治疗可能通过影响醛固酮水平, 进而影响胰岛素的敏感性。但目前相关的研究很少, 且缺乏前瞻性研究的证据。

本研究发现APA组与IHA组患者治疗前的脂代谢无明显差异, 这与OHNO等[14]研究结果一致, 而ZHU等[15]发现单侧病变的原醛症患者具有更低的TG、LDL-C及TC水平。治疗后, 两组患者均出现TG水平明显升高, 同时伴随肾功能显著下降; 进一步分析提示TG升高与螺内酯治疗、高BMI及高肌酐水平相关。ADOLF等[16]的研究也考虑TG升高与肾功能下降两者相关。本研究还发现治疗后IHA组TG更高, HDL-C更低, 提示与接受手术治疗相比, 螺内酯治疗可能带来更差的脂代谢转归。

原醛症患者治疗后糖脂代谢不良转归与心脑血管结局之间的关系尚未得到验证。既往研究表明接受MRA治疗的患者远期心血管事件及死亡风险要高于血压水平相当的EH患者, 认为与MRA治疗后PRA仍处于抑制状态〔<1 μg/(L·h)〕有关, 该研究还发现MRA治疗后患者糖尿病风险高于原发性高血压患者[17], 但未进一步分析其与心血管事件的关系。糖尿病可增加原醛症患者心脑血管事件的发生风险[18], 手术治疗可显著降低新发糖尿病风险[12], 但上述研究均未涉及治疗后代谢转归与心脑血管并发症的关系。

此外, 本研究还发现不论采取哪种治疗方案, 原醛症患者治疗后均出现肾功能明显恶化, 与其他研究结果一致[19]。目前认为治疗后患者肾功能在短期内出现恶化, 可能是由于治疗前醛固酮高分泌引起肾脏血流动力学改变, 肾小球处于超滤过状态, 掩盖了患者真实的肾功能情况, 而手术或MRA治疗阻断了醛固酮作用, 解除了上述状态, 出现e-GFR下降。多因素回归分析发现治疗后e-GFR水平还与治疗前K-min独立相关, 提示既往严重低钾对治疗后患者肾功能仍有影响。HUNDEMER等[20]发现MRA治疗后患者患慢性肾脏病(chronic kidney disease, CKD)的风险高于年龄、基础肾功能可比的原发性高血压患者, 而手术治疗患者发生CKD风险或每年e-GFR下降程度与原发性高血压患者无明显差异, 上述差异在治疗后第2年及以后逐渐显现, 提示手术治疗可能对原醛症患者远期肾功能有益。

由于本研究为回顾性研究, 平均随访时间较短, 观察指标较少, 因此未能分析造成治疗后糖脂代谢改变的可能机制。未来应设计大样本的前瞻性研究进一步明确螺

内酯或其他种类MRA治疗对糖脂代谢的影响,分析治疗后代谢转归与心脑血管并发症的关系,并探索其发生机制,以期为原醛症患者的长期优化治疗提供依据。

综上,本研究发现,原醛症患者,特别是IHA患者采用螺内酯治疗后出现显著的糖脂代谢的恶化及肾功能的下降,其发生机制及是否与长期心血管预后有关值得进一步研究。因此,对原醛症患者应尽可能明确分型,APA患者行单侧肾上腺切除手术以最大程度降低心脑血管及肾脏损害风险;而采用螺内酯治疗的患者应强调血压达标的同时保持良好的生活方式,以尽量避免出现糖脂代谢的恶化,并终身规律随访,确保能够及时应对可能出现的糖脂代谢异常。

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