

· 临床研究 ·

高龄原发性高血压患者合并慢性肾脏病的危险因素

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【摘要】目的 了解 80 岁以上原发性高血压(EH)住院患者合并慢性肾脏病(CKD)的情况,分析相关危险因素。

方法 选取南京医科大学第二附属医院心血管内科住院的 1 555 例 65 岁以上 EH 患者,依据是否≥80 岁分为 2 组:高龄组($n=575$)和非高龄组($n=980$)。收集患者的临床资料。采用 SPSS 22.0 软件进行数据处理,logistic 回归分析 EH 合并 CKD 的危险因素。**结果** 与非高龄 EH 组患者比较,高龄 EH 组患者 CKD 发生率显著升高($52.9\% \text{ vs } 29.5\%, P < 0.05$)。高龄 EH 患者合并 CKD 的危险因素依次为高尿酸血症($OR = 2.514, 95\% CI 1.750 \sim 3.611; P < 0.001$)、年龄($OR = 1.072, 95\% CI 1.018 \sim 1.129; P = 0.009$)和收缩压($OR = 1.019, 95\% CI 1.011 \sim 1.028; P < 0.001$),保护因素为高密度脂蛋白胆固醇($OR = 0.516, 95\% CI 0.315 \sim 0.847; P = 0.009$);非高龄老年 EH 患者合并 CKD 的危险因素依次为高尿酸血症($OR = 2.729, 95\% CI 1.991 \sim 3.740; P < 0.001$)、糖尿病($OR = 1.944, 95\% CI 1.420 \sim 2.662; P < 0.001$)、年龄($OR = 1.140, 95\% CI 1.101 \sim 1.182; P < 0.001$)和收缩压($OR = 1.009, 95\% CI 1.003 \sim 1.016; P = 0.007$),保护因素为高密度脂蛋白胆固醇($OR = 0.448, 95\% CI 0.278 \sim 0.722; P = 0.001$)。**结论** 高龄老年 EH 患者合并 CKD 的比例显著高于非高龄老年 EH 患者,高龄 EH 患者合并 CKD 与高尿酸血症、年龄、收缩压及高密度脂蛋白胆固醇水平有关。

【关键词】 老年人,80 以上;高血压;慢性肾脏病;危险因素

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Risk factors for essential hypertension complicated with chronic kidney disease in ≥80 years old patients

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【Abstract】 Objective To analyze the risk factors for chronic kidney disease (CKD) complication in essential hypertension (EH) patients ≥80 years of age. **Methods** A total of 1 555 elderly EH patients aged over 65 years old admitted to our department during March 2014 and June 2017 were enrolled in this study. They were assigned into ≥80-year-old group ($n=575$) and <80-year-old group ($n=980$). Their clinical data were collected and analyzed. SPSS statistics 22.0 was used to analyze the data, and logistic regression analysis was employed to identify the risk factors for CKD. **Results** Compared with <80-year-old group, ≥80-year-old group had significantly higher incidence of CKD ($52.9\% \text{ vs } 29.5\%, P < 0.05$). In ≥80-year-old EH patients, the risk factors for CKD were hyperuricemia ($OR = 2.514, 95\% CI 1.750 \sim 3.611; P < 0.001$), age ($OR = 1.072, 95\% CI 1.018 \sim 1.129; P = 0.009$) and systolic blood pressure ($OR = 1.019, 95\% CI 1.011 \sim 1.028; P < 0.001$), and the protective factor was high-density lipoprotein cholesterol ($OR = 0.516, 95\% CI 0.315 \sim 0.847; P = 0.009$). While, for <80-year-old EH patients, the risk factors were hyperuricemia ($OR = 2.729, 95\% CI 1.991 \sim 3.740; P < 0.001$), diabetes mellitus ($OR = 1.944, 95\% CI 1.420 \sim 2.662; P < 0.001$), age ($OR = 1.140, 95\% CI 1.101 \sim 1.182; P = 0.009$) and systolic blood pressure ($OR = 1.009, 95\% CI 1.003 \sim 1.016; P = 0.007$), and the protective factor was high-density lipoprotein cholesterol ($OR = 0.448, 95\% CI 0.278 \sim 0.722; P = 0.001$). **Conclusion** The incidence rate of CKD in ≥80-year-old EH patients is obviously higher than that in <80-year-old EH patients. The complication of CKD is associated with age, hyperuricemia, systolic blood pressure and high-density lipoprotein cholesterol in ≥80-year-old EH patients.

【Key words】 aged, 80 and over; hypertension; chronic kidney disease; risk factor

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我国已进入老龄化社会。2013年的数据显示,80岁以上人口超过2 300万,预计2020年将达到3 067万^[1]。近期对高龄住院患者的慢性病统计显示,高龄患者的高血压患病率为72.51%^[2]。肾脏是高血压最常见的受损靶器官。我们此前的研究显示,老年原发性高血压(essential hypertension,EH)患者的慢性肾脏病(chronic kidney disease,CKD)患病率显著高于非老年EH患者,CKD的发病与血糖、血尿酸及收缩压水平有关^[3]。然而,关于80岁以上EH患者的CKD患病情况和危险因素分析的相关研究报道十分少见。为此,我们回顾性分析了南京医科大学第二附属医院575例高龄住院EH患者的临床资料,探讨高龄EH合并CKD的患病情况及危险因素,为其诊治提供依据。

1 对象与方法

1.1 研究对象

入选2014年3月至2017年6月在我院心血管内科住院的EH患者1 555例。入选标准:(1)≥65岁;(2)EH,包括服降压药及未服药;(3)一般资料完整。排除标准:(1)继发性高血压;(2)明确肾病史;(3)服用影响血肌酐药物;(4)泌尿系统结石、感染;(5)急、慢性传染性疾病;(6)恶性肿瘤及免疫性疾病;(7)合并急性心肺功能衰竭等急症。依据是否≥80岁分为2组:高龄组($n=575$)和非高龄组($n=980$)。高龄组年龄80~97(83.9±3.4)岁,其中男性236例,女性339例;非高龄组年龄65~79(72.0±4.4)岁,其中男性433例,女性547例。

1.2 方法

详细收集并记录入选者的相关资料。入院第2天,患者晨起服用药物前平静休息10 min,取坐位采用台式水银血压计测量右臂动脉血压,连续测量3次,每次间隔5 min,取均值记录。

空腹12 h,留取患者晨尿10 ml并抽取静脉血3 ml,送检验科化验。按照简化肾病饮食改良方程公式计算估算肾小球滤过率(estimated glomerular filtration rate,eGFR), $eGFR = 186 \times 血清肌酐^{-1.154} \times 年龄^{-0.203} \times 性别系数$ (男性1,女性0.742)。本研究所有记录项目均为患者入院后的第1次化验数值,如患者住院数次,均以第1次住院时检测结果为准。

1.3 诊断标准

EH:未服用降压药情况下,非同日和(或)连续3次测量血压,平均收缩压≥140 mmHg(1 mmHg=0.133 kPa)和(或)舒张压≥90 mmHg;既往有高血压病史,服药后虽然血压<140/90 mmHg,也诊断为高血

压。eGFR下降:eGFR<60 ml/(min·1.73 m²)。CKD:(1)蛋白尿:24 h尿微量白蛋白≥300 mg或尿蛋白≥1个+;(2)eGFR下降:eGFR<60 ml/(min·1.73 m²)。糖尿病:(1)空腹血糖≥7.0 mmol/L或餐后2 h血糖≥11.1 mmol/L;(2)既往有糖尿病史。高尿酸血症:血尿酸男性>420 μmol/L、女性>360 μmol/L或使用降尿酸药物。

1.4 统计学处理

采用SPSS 22.0软件进行数据处理。计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用t检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。采用多因素logistic回归分析危险因素。 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 2组患者一般临床资料比较

与非高龄EH组患者比较,高龄EH组患者的肌酐和尿酸显著升高,冠心病、高尿酸血症、蛋白尿、eGFR下降和CKD发生率也显著升高($P<0.05$),而舒张压、空腹血糖、甘油三酯、总胆固醇、低密度脂蛋白胆固醇和eGFR显著降低($P<0.05$;表1)。

2.2 2组患者中不同性别CKD发生率比较

2组患者中男性CKD发生率均显著高于女性,但差异无统计学意义($P>0.05$;表2)。

2.3 高龄组不同收缩压水平患者蛋白尿、eGFR下降和CKD构成比比较

高龄组中不同收缩压水平患者的蛋白尿及CKD发生率间差异具有统计学意义($P<0.001$;表3)。

2.4 logistic回归分析EH合并CKD危险因素

根据上述资料,以是否合并CKD为因变量,以年龄、性别、收缩压水平、胆固醇、冠心病史、糖尿病史等为自变量,行logistic回归分析。结果表明,高龄EH患者合并CKD的危险因素依次为高尿酸血症($OR=2.514, 95\% CI 1.750\sim3.611; P<0.001$)、年龄($OR=1.072, 95\% CI 1.018\sim1.129; P=0.009$)、收缩压($OR=1.019, 95\% CI 1.011\sim1.028; P<0.001$),保护因素为高密度脂蛋白胆固醇($OR=0.516, 95\% CI 0.315\sim0.847; P=0.009$;表4,表5);非高龄老年EH患者合并CKD的危险因素依次为高尿酸血症($OR=2.729, 95\% CI 1.991\sim3.740; P<0.001$)、糖尿病($OR=1.944, 95\% CI 1.420\sim2.662; P<0.001$)、年龄($OR=1.140, 95\% CI 1.101\sim1.182; P<0.001$)、收缩压($OR=1.009, 95\% CI 1.003\sim1.016; P=0.007$),保护因素为高密度脂蛋白胆固醇($OR=0.448, 95\% CI 0.278\sim0.722; P=0.001$;表6,表7)。

表1 2组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	≥80-year-old group (n=575)	<80-year-old group (n=980)	P value
SBP(mmHg, $\bar{x} \pm s$)	143.39±22.54	144.70±22.44	0.266
DBP(mmHg, $\bar{x} \pm s$)	79.72±11.85	83.28±11.27	<0.001
FBG(mmol/L, $\bar{x} \pm s$)	6.06±2.37	6.36±2.59	0.024
TG(mmol/L, $\bar{x} \pm s$)	1.32±0.77	1.59±1.05	<0.001
TC(mmol/L, $\bar{x} \pm s$)	4.14±1.15	4.33±1.12	0.001
HDL-C(mmol/L, $\bar{x} \pm s$)	1.22±0.37	1.22±0.36	0.967
LDL-C(mmol/L, $\bar{x} \pm s$)	2.25±0.77	2.40±0.79	<0.001
Urea(μmol/L, $\bar{x} \pm s$)	7.72±4.65	7.02±12.88	0.206
Creatinine(μmol/L, $\bar{x} \pm s$)	100.57±59.23	87.25±57.01	<0.001
eGFR[ml/(min·1.73 m ²), $\bar{x} \pm s$]	66.35±26.69	79.12±24.71	<0.001
UA(μmol/L, $\bar{x} \pm s$)	367.17±116.20	344.83±105.36	<0.001
CHD[n(%)]	432(75.1)	651(66.4)	<0.001
DM[n(%)]	152(26.5)	300(30.6)	0.083
Hyperuricemia[n(%)]	221(38.4)	275(28.1)	<0.001
Albuminuria[n(%)]	164(28.5)	185(18.9)	<0.001
Declined eGFR[n(%)]	220(38.3)	164(16.7)	<0.001
CKD[n(%)]	304(52.9)	289(29.5)	<0.001

SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; UA: uric acid; CHD: coronary heart disease; DM: diabetes mellitus; CKD: chronic kidney disease. 1 mmHg = 0.133 kPa.

表2 不同性别患者CKD发生率比较

Table 2 Comparison of incidence of CKD between different gender groups

Group	n	Male		χ^2	P value
		n	CKD[n(%)]		
≥80-year-old	575	236	134(56.8)	339	170(50.1)
<80-year-old	980	433	129(29.8)	547	160(29.3)

CKD: chronic kidney disease.

表3 高龄组不同收缩压水平患者蛋白尿、eGFR下降、CKD构成比比较

Table 3 Comparison of albuminuria, declined eGFR and CKD with different systolic blood pressure levels in ≥80-year-old group
[n(%)]

SBP(mmHg)	n	Albuminuria	Declined eGFR	CKD
<120	53	8(15.1)	21(39.6)	26(49.1)
120~139	183	36(19.7)	64(35.0)	79(43.2)
140~159	184	47(25.5)	66(35.9)	93(50.5)
160~179	101	40(39.6)	46(45.5)	64(63.4)
≥180	54	33(61.1)	23(42.6)	42(77.8)
χ^2		46.734	4.022	25.531
P value		<0.001	0.403	<0.001

eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease; SBP: systolic blood pressure. 1 mmHg = 0.133 kPa.

表4 高龄老年EH患者合并CKD危险因素的单因素logistic回归分析

Table 4 Univariate logistic regression analysis of risk factors of CKD in ≥80-year-old EH patients

Factor	B	SE	χ^2	OR	95%CI	P value
Age	0.073	0.027	7.253	1.075	1.020~1.133	0.007
SBP	0.021	0.005	17.376	1.021	1.011~1.031	<0.001
HDL-C	-0.514	0.287	3.204	0.598	0.340~1.050	0.050
Hyperuricemia	0.976	0.189	26.535	2.654	1.831~3.847	<0.001

EH: essential hypertension; CKD: chronic kidney disease; SBP: systolic blood pressure; HDL-C: high-density lipoprotein cholesterol.

表5 高龄老年EH患者合并CKD危险因素的多因素logistic回归分析

Table 5 Multivariate logistic regression analysis of risk factors of CKD in ≥80-year-old EH patients

Factor	B	SE	χ^2	OR	95%CI	P value
Hyperuricemia	0.922	0.185	24.898	2.514	1.750~3.611	<0.001
Age	0.069	0.027	6.848	1.072	1.018~1.129	0.009
SBP	0.019	0.004	20.909	1.019	1.011~1.028	<0.001
HDL-C	-0.661	0.253	6.840	0.516	0.315~0.847	0.009

EH: essential hypertension; CKD: chronic kidney disease; SBP: systolic blood pressure; HDL-C: high-density lipoprotein cholesterol.

表6 非高龄老年EH患者合并CKD危险因素的单因素logistic回归分析

Table 6 Univariate logistic regression analysis of risk factors of CKD in <80-year-old EH patients

Factor	B	SE	χ^2	OR	95%CI	P value
Age	0.131	0.019	49.891	1.140	1.099~1.182	<0.001
SBP	0.009	0.004	4.753	1.009	1.001~1.018	0.029
HDL-C	-0.857	1.004	7.036	0.424	0.225~0.799	0.008
Hyperuricemia	1.042	2.004	40.717	2.836	2.059~3.906	<0.001
DM	0.615	3.004	10.324	1.849	1.271~2.690	0.001

EH: essential hypertension; CKD: chronic kidney disease; DM: diabetes mellitus; SBP: systolic blood pressure; HDL-C: high-density lipoprotein cholesterol.

表7 非高龄老年EH患者合并CKD危险因素的多因素logistic回归分析

Table 7 Multivariate logistic regression analysis of risk factors of CKD in <80-year-old EH patients

Factor	B	SE	χ^2	OR	95%CI	P value
Hyperuricemia	1.004	0.161	38.948	2.729	1.991~3.740	<0.001
DM	0.665	0.160	17.192	1.944	1.420~2.662	<0.001
Age	0.131	0.018	52.893	1.140	1.101~1.182	<0.001
SBP	0.009	0.003	7.379	1.009	1.003~1.016	0.007
HDL-C	-0.803	0.243	10.897	0.448	0.278~0.722	0.001

EH: essential hypertension; CKD: chronic kidney disease; DM: diabetes mellitus; SBP: systolic blood pressure; HDL-C: high-density lipoprotein cholesterol.

3 讨论

随着生活水平提高和生活方式的改变,高龄人群的高血压患病率逐渐升高。高血压是CKD最常见的合并症。美国肾脏早期评估项目KEEP的研究结果显示,86.2%的CKD患者同时患有高血压^[4]。CKD患者因水钠潴留、肾素水平升高、交感神经活性增高、内皮细胞功能障碍而血压升高。而高血压也是导致终末期肾病的主要原因之一。因此,对于高龄EH患者CKD发病率及相关危险因素的研究十分必要。我们的研究初步显示,高龄组患者的蛋白尿、eGFR下降及CKD检出率均显著高于非高龄组患者。与非高龄老人相比,高龄老人存在着肝、肾等器官老化更严重、代谢功能更差、机体更容易处于慢性炎症状态等特点,因此尿素、肌酐、尿酸、冠心病、高尿酸血症、蛋白尿、eGFR下降、CKD发生率明显升高。另外,本研究结果显示,高龄组的空腹血糖、甘油三酯、总胆固醇及低密度脂蛋白胆固醇相较于非高龄组显著降低,未出现随着年龄增长而空腹血糖增高、血脂紊乱的趋势,这与吕宪玉

等^[5]的研究数据相符。

有报道,收缩压水平是中晚期老年CKD患者肾功能快速进展的独立危险因素^[6]。本研究发现,高龄组收缩压每升高20 mmHg,蛋白尿及CKD的构成比亦显著升高。收缩压越高,肾小球内压增高越明显,肾小球滤过率增加,同时肾小球内压增高可引起血管紧张素Ⅱ、内皮素-1和多种生长因子及炎症介质释放,加重肾损害。有研究结果显示,对于收缩压为160~199 mmHg的≥80岁患者,将血压控制在150/80 mmHg以下,脑卒中病死率可降低30%,心力衰竭发生率可降低64%,全因死亡率可降低21%^[7]。高龄老年人血压管理中国专家共识指出:高龄老人,健康状态良好者,建议将血压控制在150/90 mmHg以内;能够耐受者,建议血压降至<140/90 mmHg^[1]。

年龄是eGFR下降的独立危险因素,我们的研究也表明,高龄组患者的eGFR下降水平明显高于非高龄组。但本研究结果亦显示高龄组患者蛋白尿的发生率明显高于非高龄组,表明高龄老人eGFR的下降除了生理因素外,还受疾病等外界因素的影

响,其中蛋白尿增多是高龄老年 EH 患者肾功能减退的一个重要因素。一项针对韩国>65岁老年人的调查发现,肾功能减退和蛋白尿是全因死亡的独立危险因素^[8]。蛋白尿减少预示着 CKD 进展减缓,甚至心血管事件发生率减低^[9]。因此,重视蛋白尿的治疗对于改善高龄老人人群预后具有积极意义。

本研究对高龄老人及非高龄老人 EH 患者合并 CKD 进行危险因素分析,结果提示高尿酸血症是重要的危险因素,而高密度脂蛋白胆固醇则是保护因素。众所周知,高尿酸血症可造成肾小管内皮细胞损伤,导致蛋白尿产生,是 CKD 进展的重要因素^[10,11]。降尿酸治疗有利于减少高龄老人 EH 患者心脑血管事件的发生,并延缓 CKD 进展。高密度脂蛋白胆固醇可运载周围组织中的胆固醇至肝脏组织,促进细胞内胆固醇的清除,限制动脉粥样硬化发生。有研究表明,甘油三酯/高密度脂蛋白胆固醇比值升高是 CKD 患者发生大量蛋白尿的独立危险因素^[12]。

糖尿病通常是 CKD 的重要危险因素之一。本研究结果显示,在非高龄老人人群中,糖尿病是 EH 合并 CKD 的危险因素。但我们研究结果也显示,相对于非高龄老人 EH 患者,高龄老人 EH 患者的糖尿病发病率反而有所下降,进一步分析显示,在高龄老人人群中,糖尿病不再是 EH 合并 CKD 的危险因素。对于高龄老人糖尿病的治疗,低血糖尤其是夜间低血糖是难点。有研究显示,强化降糖可使全因死亡率增加 21%~31%,其中低血糖和心血管疾病是导致死亡的主要原因^[13~15]。因此,对于高龄老人患者的降糖方案应以安全为先,合理用药,个体化治疗,做到优化降糖与尽量降低低血糖风险。

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