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高通量血液透析对糖尿病肾病血液透析患者心脏功能及结构的影响及预后的影响因素分析*

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摘要 目的:探讨高通量血液透析对糖尿病肾病(DN)血液透析患者心脏功能及结构的影响,并分析预后的影响因素。**方法:**选取2017年5月~2018年11月期间我院收治的DN血液透析患者(n=172),上述DN血液透析患者中普通透析治疗者60例(普通透析组)、高通量血液透析治疗者112例(高通量透析组)。普通透析组采用低通量透析治疗,高通量透析组采用高通量透析治疗,比较两组患者心脏功能及结构以及预后情况,采用单因素、多因素 Logistic 回归分析预后的影响因素。**结果:**高通量透析组治疗6个月后左心房内径(LAD)、左心室舒张末内径(LVDd)、左心室心肌重量指数(LVMI)低于治疗前和普通透析组($P<0.05$),高通量透析组治疗6个月后左心室射血分数(LVEF)高于治疗前和普通透析组($P<0.05$)。高通量透析组的生存率高于普通透析组($P<0.05$)。存活组年龄、上机前舒张压、上机前收缩压、血磷、全段甲状旁腺激素(iPTH)均低于死亡组($P<0.05$),存活组透析频率、白蛋白、血红蛋白均高于死亡组($P<0.05$),两组性别、血钙比较无差异($P>0.05$)。多因素 Logistic 回归分析结果显示,上机前舒张压高、上机前收缩压高、血磷高、iPTH高、透析频率少、白蛋白低、血红蛋白低均是DN血液透析患者死亡的危险因素($P<0.05$)。**结论:**高通量血液透析能减轻DN患者血液透析所引起的心脏功能及结构损伤,改善患者预后。影响DN血液透析患者预后的因素较多,其中上机前舒张压、上机前收缩压、血磷、iPTH越高,白蛋白、血红蛋白越低,透析频率越少,患者的死亡风险越大。

关键词:高通量血液透析;糖尿病肾病;血液透析;心脏功能;心脏结构;预后

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The Influence of High Flux Hemodialysis on Cardiac Function and Structure and the Influencing Factors of Prognosis in Hemodialysis Patients with Diabetic Nephropathy*

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ABSTRACT Objective: To investigate the effect of high flux hemodialysis on cardiac function and structure in hemodialysis patients with diabetic nephropathy (DN), and to analyze the prognostic factors. **Methods:** The clinical data of DN hemodialysis patients (n = 172) admitted to our hospital from May 2017 to November 2018 were retrospectively selected. Among the above-mentioned DN hemodialysis patients, 60 patients were treated with common dialysis (common dialysis group) and 112 patients were treated with high-throughput hemodialysis (high-throughput dialysis group). The common dialysis group was treated with low-throughput dialysis, while the high-throughput dialysis group was treated with high-throughput dialysis. Single factor and Multivariate Logistic regression were used to analyze influencing factors of prognosis. **Results:** 6 months after treatment, left atrial diameter (LAD), left ventricular end-diastolic diameter (LVDd) and left ventricular myocardial mass index (LVMI) of the high-throughput dialysis group were lower than those of the before treatment and common dialysis group ($P<0.05$), and left ventricular ejection fraction (LVEF) of the high-throughput dialysis group was higher than that of the before treatment and common dialysis group ($P<0.05$). The survival rate of the high-throughput dialysis group was higher than that of the common dialysis group ($P<0.05$). Age, pre-operative diastolic blood pressure, pre-operative systolic blood pressure, blood phosphorus, and full parathyroid hormone (iPTH) of the survival group were all lower than those of the death group ($P<0.05$), and the dialysis frequency, albumin, and hemoglobin of the survival group were all higher than those of the death group ($P<0.05$). There were no significant differences between the two groups in gender and blood calcium ($P>0.05$). Multivariate Logistic regression analysis showed that high diastolic blood pressure, high systolic blood pressure before admission, high blood phosphorus, high iPTH, low dialysis frequency, low albumin and low hemoglobin were all risk factors for death in hemodialysis patients with DN ($P<0.05$). **Conclusion:** High flux hemodialysis can reduce the cardiac function and structural damage caused by hemodialysis patients with DN, and improve the prognosis of patients. There are many factors affecting the prognosis of hemodialysis patients with

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DN, among which, the higher diastolic blood pressure, the higher preoperative systolic blood pressure, blood phosphorus and iPTH, the lower the albumin and hemoglobin, and the lower the dialysis frequency, the greater the risk of death.

Key words: High flux hemodialysis; Diabetic nephropathy; Hemodialysis; Cardiac function; Cardiac structure; Prognosis

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前言

糖尿病是一组以高血糖为特征的代谢性疾病,患者体内脂肪、糖、蛋白、水等一系列代谢紊乱,若血糖长期控制不佳,可引起多个系统损害^[1-3]。糖尿病肾病(DN)是糖尿病患者的常见并发症之一,是导致患者肾衰竭的主要原因^[4-5]。据统计^[6],DN导致的肾衰竭占慢性肾衰竭总发病率的27%。血液透析是治疗DN的主要方法,可有效提高患者生存率^[7]。然而,血液透析也面临着巨大挑战。有研究显示^[8],透析患者每年的死亡率高达24%,其中最主要的死亡原因为心血管疾病,远期预后差。鉴于此,本文拟通过观察高通量血液透析对DN血液透析患者心脏功能及结构的影响,并分析预后的影响因素,旨在为临床DN血液透析患者治疗提供数据参考。

1 资料与方法

1.1 一般资料

选取2017年5月~2018年11月期间我院收治的DN血液透析患者172例,纳入标准:(1)DN的诊断标准参考《糖尿病肾病防治专家共识(2014年版)》^[9];(2)均符合血液透析治疗指征者;(3)肾小球滤过率升高 $\geq 20\%$,24h尿蛋白定量 ≤ 3.0 g,尿蛋白排泄率为20~200 $\mu\text{g}/\text{min}$;(4)临床资料完整;(5)每周透析次数为3次,每次4h,透析时间 >3 个月。排除标准:(1)妊娠或哺乳期妇女;(2)合并结核、肿瘤等慢性消耗性疾病者;(3)合并精神疾患,无法配合治疗者;(4)合并创伤、感染等急性临床事件。上述DN血液透析患者中普通透析治疗者60例(普通透析组)、高通量血液透析治疗者112例(高通量透析组)。我院医学伦理委员会已批准进行本研究,所有患者均签署同意书。

1.2 治疗方法

普通透析组采用低通量F6透析器,材料为聚砜膜,膜面积1.3 m^2 ,超滤系数5.5 $\text{mL}/(\text{h}\cdot\text{mmHg})$ 。高通量透析组采用高通量FX60透析器,材料为聚砜膜,超滤系数40 $\text{mL}/(\text{h}\cdot\text{mmHg})$ 、膜面积1.3 m^2 。均统一使用威高空心纤维F15透析器(CTA-2000CH),透析液流量500 mL/min ,血流量250~300 mL/min ,

每周透析3次,每次4h,FX60平均复用10次,F6平均复用6次,实验周期6个月,低分子肝素钠抗凝。

1.3 观察指标

(1)临床资料:收集上机前舒张压、年龄、性别、上机前收缩压、透析频率等临床资料。(2)临床指标:在例行血液透析当日透析前空腹留取4 mL 血液标本,经常规离心处理(2800 r/min 的离心转速,离心半径12 cm ,离心15 min)分离血清,置于低温冰箱中待测。采用贝克曼库尔特奥林巴斯AU-5400型血生化全自动分析仪检测白蛋白、血钙、血磷;采用化学发光法测定全段甲状旁腺激素(iPTH),试剂盒选用西门子iPTH测定试剂盒;采用希森美康医用电子(上海)有限公司生产的全自动血液分析仪检测血红蛋白。(3)心脏功能及结构:采用IU22型多普勒超声心动仪检测治疗前和治疗6个月后的左心室射血分数(LVEF)、左心室舒张末内径(LVDd)、左心房内径(LAD)、左心室心肌重量指数(LVMI)。探头频率2.5~3.5 MHz 。(4)预后:采用门诊复查、电子通信等随访方式对所有透析治疗患者进行随访1年,记录两组患者预后情况。根据预后将所有血液透析治疗患者分为死亡组($n=16$)和存活组($n=156$)。随访终止指征为患者死亡或随访到截止日期。

1.4 统计学方法

采用SPSS 20.0统计软件进行分析,计数资料采用 χ^2 检验,用%表示。计量资料以 $(\bar{x}\pm s)$ 表示,采用t检验,采用单因素及多因素Logistic回归分析预后的影响因素。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 两组心脏功能及结构相关指标比较

两组治疗前LAD、LVDd、LVEF、LVMI比较差异无统计学意义($P>0.05$),普通透析组治疗前、治疗6个月后LAD、LVDd、LVEF、LVMI组内比较差异无统计学意义($P>0.05$),高通量透析组治疗6个月后LAD、LVDd、LVMI低于治疗前和普通透析组($P<0.05$),高通量透析组治疗6个月后LVEF高于治疗前和普通透析组($P<0.05$),详见表1。

表1 两组心脏功能及结构相关指标比较($\bar{x}\pm s$)

Table 1 Comparison of cardiac function and structure indexes between the two groups($\bar{x}\pm s$)

Groups	Time	LAD(mm)	LVDd(mm)	LVEF(%)	LVMI(g/cm ²)
Common dialysis group (n=60)	Before treatment	40.12 \pm 3.19	54.92 \pm 4.21	55.03 \pm 4.16	162.33 \pm 18.19
	6 months after treatment	38.96 \pm 3.56	54.38 \pm 5.31	55.98 \pm 4.03	161.29 \pm 15.23
High-throughput dialysis group(n=112)	Before treatment	40.08 \pm 2.96	55.03 \pm 5.23	55.09 \pm 4.22	162.07 \pm 16.23
	6 months after treatment	34.51 \pm 2.85 ^{ab}	50.17 \pm 6.24 ^{ab}	60.07 \pm 5.17 ^{ab}	154.53 \pm 21.28 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with the common dialysis group, ^b $P<0.05$.

2.2 两组预后情况比较

普通透析组随访到期后死亡人数 10 例,存活 50 例,生存率为 83.33%(50/60);高通量透析组随访到期后死亡人数 6 例,存活 106 例,生存率为 94.64%(106/112);高通量透析组的生存率高于普通透析组($\chi^2=5.923, P=0.015$)。

2.3 DN 血液透析患者预后的单因素分析

存活组年龄、上机前舒张压、上机前收缩压、血磷、iPTH 均低于死亡组($P<0.05$),存活组透析频率、白蛋白、血红蛋白均高于死亡组($P<0.05$),两组性别、血钙比较无统计学差异($P>0.05$),详见表 2。

表 2 DN 血液透析患者预后的单因素分析

Table 2 Single factor analysis of the prognosis of hemodialysis patients with DN

Indexes	Death group(n=16)	Survival group (n=156)	χ^2/t	P
Age(years)	64.57±5.39	53.42±7.03	7.167	0.000
Gender(male/female)	10/6	81/75	0.652	0.420
Pre-operative diastolic blood pressure(mmHg)	97.73±7.03	86.39±6.38	7.609	0.000
Pre-operative systolic blood pressure(mmHg)	119.28±11.86	92.73±10.84	10.500	0.000
Dialysis frequency(times / week)	1.74±0.29	2.45±0.31	10.088	0.000
Albumin(g/L)	28.11±3.79	37.02±2.37	14.576	0.000
Blood calcium(g/mL)	2.19±0.22	2.23±0.21	0.823	0.412
Blood phosphorus(g/mL)	1.79±0.31	1.46±0.29	4.900	0.000
iPTH(pg/mL)	512.96±29.21	396.44±31.34	16.386	0.000
Hemoglobin(g/L)	84.43±7.32	98.40±8.03	7.693	0.000

2.4 DN 血液透析患者预后的多因素分析

以 DN 血液透析患者存活情况作为因变量(赋值:存活=0、死亡=1),将单因素分析结果中有统计学意义的指标:年龄、上机前舒张压、上机前收缩压、血磷、iPTH、透析频率、白蛋

白、血红蛋白作为自变量纳入多因素 Logistic 回归分析,结果显示,上机前舒张压高、上机前收缩压高、血磷高、iPTH 高、透析频率少、白蛋白低、血红蛋白低均是 DN 血液透析患者死亡的危险因素。详见表 3。

表 3 DN 血液透析患者预后的多因素分析

Table 3 Multivariate analysis of prognosis of hemodialysis patients with DN

Variables	β	SE	Wald χ^2	P	OR	OR 95%CI
High pre-operative diastolic blood pressure	0.879	0.338	6.653	0.011	2.409	1.226~4.718
High pre-operative systolic blood pressure	0.758	0.328	5.163	0.022	2.127	1.126~4.128
High blood phosphorus	1.268	0.414	9.813	0.000	3.576	1.608~7.937
High iPTH	1.039	0.316	10.937	0.000	1.347	1.186~1.642
Low dialysis frequency	0.728	0.313	5.866	0.013	2.115	1.253~3.768
Low hemoglobin	0.609	0.248	4.421	0.035	1.847	1.165~3.183
Low albumin	0.865	0.313	8.127	0.003	2.437	1.325~4.438

3 讨论

血液透析是一个长期治疗过程,随着治疗时间的延长,各类并发症也随之发生^[10-12]。有研究表明,血液透析患者存在胰岛素抵抗,极易引起心血管相关疾病的发生,严重者可导致死亡^[13-15]。目前使用的血液透析器种类较多,根据透析器的超滤系数分为低通量透析器、高通量透析器。近年来有研究证实^[16],血液透析患者的并发症发生风险与透析方式息息相关,本研究就此展开分析。

本次研究结果显示,高通量透析组治疗 6 个月后 LAD、

LVDd、LVMI 低于普通透析组而 LVEF 则高于普通透析组,同时对两组预后发现,高通量透析组的生存率高于普通透析组。表明高通量透析可减轻对人体心脏功能及结构的损害,改善患者生存率。由于心血管并发症的发生与人体内中大分子物质的残留息息相关,低通量透析器对中大分子物质的清除效果较差或难以清除^[17-19]。而高通量透析器因其透析系数高、透析膜表面积大,具备更高的通透性及溶质扩散性能,可有效清除中大分子物质,进而减轻氧化应激、炎症反应及血管内皮变化等,提高患者生存率^[20-22]。

国内研究报道显示^[23],DN 是血液透析尿毒症患者死亡的

独立危险因素。因此,研究 DN 患者的死亡危险因素,并对相关危险因素进行有目的地前瞻性干预治疗,对于改善 DN 患者预后有着重要意义。本研究中多因素 Logistic 回归分析结果显示,上机前舒张压高、上机前收缩压高、血磷高、iPTH 高、透析频率少、白蛋白低、血红蛋白低均是 DN 血液透析患者死亡的危险因素。以往研究结果证实^[24],高血压是导致心脑血管并发症的主要原因。上机前舒张压、上机前收缩压过高可引起动脉硬化、加剧左心室肥厚,最终导致患者出现出血性脑卒中、心律失常等心脑血管并发症,增加其死亡率^[25,26]。低白蛋白、低血红蛋白多见于结核、恶性肿瘤等慢性消耗性疾病,也是 DN 患者常见并发症。血液透析治疗过程中饮食控制不当、蛋白质及营养物质的丢失等均可导致低白蛋白、低血红蛋白的发生。有研究显示^[27],低蛋白血症是影响血液透析患者住院的危险因素。机体合并低白蛋白、低血红蛋白可促使血浆载脂蛋白产生异常,起机体凝血、抗凝和纤溶系统失衡,机体免疫力明显下降,导致感染几率增加,提高死亡风险。磷参与人体多项生理功能及化学反应,对维持全身骨骼系统、维持肾脏正常机能、机体能量代谢、凝血过程、传达神经刺激、调节酸碱平衡等方面发挥重要作用。当肾小球滤过率下降、尿磷排出减少,血磷升高,并引起严重并发症,影响 DN 患者的生存期、生存质量^[28]。标准的血液透析治疗方案推荐每周 3 次、每次 4 小时。由于我国医疗服务能力有限、医疗保险保障机制的不够完善、患者家庭条件不一等因素,部分 DN 患者无法完成标准的血液透析治疗方案。而增加透析频率能改善血液透析患者微炎症状态、营养状况并使感染发生风险降低,预后改善。以往也有报道表明透析频率是生存保护因素,即透析次数越多,死亡风险越小^[29]。iPTH 是血管内皮损伤的危险因子,与心血管、血管钙化相关的死亡密切联系,iPTH 越高,血管钙化和心血管等并发症几率增加,从而增加死亡几率^[30]。

综上所述,高通量血液透析能减轻 DN 患者血液透析所引起的心脏功能及结构损伤,改善患者预后。影响 DN 血液透析患者预后的因素较多,包括上机前舒张压、上机前收缩压、血磷、iPTH、透析频率、白蛋白、血红蛋白等,临床可通过监测上述指标并予以适当的干预以改善患者预后。

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