doi: 10.13241/j.cnki.pmb.2017.30.025

肾移植术后患者同型半胱氨酸、肾功能和血脂水平的变化及其相关性分析

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摘要 目的：分析肾移植术后患者血清的同型半胱氨酸（Hcy）、肾功能和血脂水平的变化和相关性，探讨其在肾移植术后评价肾功能的应用价值。**方法：**将 2013 年 10 月 ~2016 年 9 月就诊于我院确诊慢性肾衰并进行肾移植手术的 300 例术后随访患者作为观察组，选择同期健康志愿者 100 例作为对照组。检测并比较两组 Hcy、总胆固醇（TC）、三酰甘油（TG）、低密度脂蛋白胆固醇（LDL-C）、高密度脂蛋白胆固醇（HDL-C）水平。根据观察组患者 Hcy 水平的不同将其分成 Hcy 正常组与 Hcy 异常组，并对比两组患者的血脂指标水平；测定半胱氨酸蛋白抑制剂 C（CysC）的水平并计算肾小球滤过率（eGFR）；对观察组血清 Hcy 与 eGFR 值、血脂指标水平进行相关性分析，并采用 Logistic 回归分析分析观察组肾移植术后 eGFR 下降的影响因素。**结果：**观察组患者的血清 Hcy、TC、TG、HDL-C、LDL-C 水平均明显高于对照组（P＜0.05）。Hcy 异常组血清 LDL-C 水平明显高于 Hcy 正常组，而 HDL-C 水平明显低于 Hcy 正常组（P＜0.05）。观察组患者血清 Hcy 与 eGFR、HDL-C 水平呈负相关关系（r=-0.573、-0.414，P＜0.05）；与 TG 水平呈正相关（r=0.432，P＜0.05），与 TC、LDL-C 无相关（P＞0.05）。多元 Logistic 回归分析显示，Hcy、TG、LDL-C 水平均与患者 eGFR 下降有关（P＜0.05）。**结论：**在肾移植术后，慢性肾衰患者的 TG、LDL-C、Hcy 水平均升高，且伴有 eGFR 水平的降低；肾移植术后肾功能的改变与血清 TG、LDL-C、Hcy 水平相关；检测肾移植患者血脂指标、Hcy 的水平可以评估移植肾功能受损情况。

关键词：肾移植术；同型半胱氨酸；肾功能；血脂水平

中图分类号：R699 **文献标识码：**A **文章编号：**1673-6273(2017)30-5908-04

Study on Changes of Homocysteine, Renal Function and Blood Lipid Levels in Renal Transplanted Recipients

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ABSTRACT Objective: To analyze the changes of serum homocysteine (Hcy), renal function and blood lipid levels in renal transplanted recipients and their correlation, so as to investigate the application value of them in the evaluation of renal function after renal transplantation. **Methods:** A total of 300 cases of renal transplanted recipients followed up postoperatively, who were diagnosed as chronic renal failure and underwent renal transplantation in the Affiliated Hospital of Qingdao University during October 2013 to September 2016, were chosen as observation group; 100 healthy volunteers in the same period were chosen as control group.The levels of Hcy, total cholesterol (TC), three triacylglycerol (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) of the two groups were detected and compared. According to the different levels of Hcy in the observation group, the patients were further divided into Hcy normal group and Hcy abnormal group,and the blood lipid indexes of the two groups were compared. The level of cysteine protein inhibitor C (CysC) was measured and glomerular filtration rate (eGFR) was calculated. The correlation between serum Hcy and eGFR, blood lipid indexes levels in the observation group was analyzed.Logistic regression analysis was used to analyze the influencing factors of eGFR decline after renal transplantation in the observation group. **Results:** The levels of Hcy, TC, TG, HDL-C and LDL-C in the observation group were significantly higher than those in the control group (P<0.05). The level of LDL-C in Hcy abnormal group was higher than that in Hcy normal group, while the level of HDL-C was lower than that in Hcy normal group (P<0.05). The serum Hcy level of the observation group was negatively correlated with the levels of eGFR and HDL-C (r= -0.573, -0.414; P<0.05), and positively correlated with the level of TG (r=0.432, P<0.05), but was not related to TC and LDL-C (P>0.05). Multivariate Logistic regression analysis showed that the levels of Hcy, TG and LDL-C were related to the decrease of eGFR in patients (P<0.05). **Conclusion:** After renal transplantation, the TG, LDL-C and Hcy levels in patients with chronic renal failure will rise and eGFR level will drop. The change of renal function after renal transplantation is related to the levels of serum TG, LDL-C and Hcy. Detection of lipid profile and Hcy levels in renal transplant recipients can assess impaired graft function.

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(收稿日期：2017-05-31 接受日期：2017-06-25)

Key words: Renal transplantation; Homocysteine; Renal function; Blood lipid level
Chinese Library Classification(CLC): R699 Document code: A
Article ID: 1673-6273(2017)30-5908-04

前言

肾脏移植是挽救肾脏疾病终末期患者生命、提高其生活质量最有效的方法[1,2]。随着医疗技术的不断发展,肾移植受者的存活率与术后生活质量均有显著提高,CSRKT 数据库显示我国肾脏移植从 20 世纪 60 年代初始至今,我国活体肾移植数量逐年升高,肾移植术后不良反应发生率与恢复透析的数量相应增加,其中移植肾功能延迟恢复(DGF)是肾移植术后最常见也是最严重的并发症,其临床症状主要表现为:患者术后乏力、贫血、血尿、血清肌酐水平增高等[3,4]。DGF 的发生增加了患者肾移植术后急性排斥反应的发生率,大大缩短了移植肾的存活时间[5,6]。有学者研究表明高脂血症是慢性移植肾功能衰竭的危险因素[7,8]。同时同型半胱氨酸(Hcy)作为一种含硫氨基酸,也被广泛认为是心血管疾病的独立危险因素,其水平的升高也能够引起肾功能的损害[9,10]。本文通过对肾移植术后患者血清的 Hcy、血脂指标水平与肾功能的相关性分析,发现在肾移植患者体内 Hcy、TG、LDL-C 水平均与患者 eGFR 下降有关,现报告如下。

1 资料与方法

1.1 一般资料

将 2013 年 10 月 ~2016 年 9 月于我院接受肾移植手术的慢性肾功能衰竭术后随访患者 300 例纳入观察组, 纳入标准:(1) 均符合慢性肾功能衰竭诊断标准 [11], 且肾小球滤过率(eGFR)<15 mL/min·1.73 m^2;(2)患者及其家属知情同意。排除标准:(1)无心、肺、脑、肝功能障碍;(2)无恶性肿瘤、糖尿病、心血管系统疾病。其中男 146 例,女 154 例,年龄 21~64 岁,平均年龄(41.37± 9.83)岁。选取在我院体检结果为健康的志愿者 100 例作为对照组,其中男 47 例,女 53 例,年龄 20~61 岁,平均年龄(39.65± 8.96)岁,两组患者性别、年龄比较,差异无统计学意义(P>0.05)。观察组患者根据 Hcy 水平分为两组,Hcy 正常组(Hcy 范围 0~15 μmol/L)167 例,其中男 80 例,女 87 例,平均年龄(40.98± 8.73)岁;与 Hcy 异常组 133 例,其中男 66 例,女 67 例,平均年龄(42.74± 10.37)岁。Hcy 正常组与 Hcy 异常组患者性别、年龄比较,差异无统计学意义(P>0.05),具有可比性。

1.2 方法

观察组、对照组分别于清晨抽取 3 mL 空腹静脉血;所有静脉血标本均注入装有肝素的抗凝管内,37℃下离心 4 min(3500 r/min),取上清液进行检测。两组静脉血均采用 ADVIA2400 全自动生化分析仪(德国西门子)检测 Hcy、肾功能、血脂指标;其中血清中胆固醇(TC)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、高密度脂蛋白胆固醇(HDL-C)、半胱氨酸蛋白酶抑制剂(CysC)试剂盒均采用西门子公司配套生产,Hcy 试剂盒为北京万泰德瑞诊断技术有限公司生产。

1.3 观察指标及评定标准

1.3.1 **观察指标** 两组观察对象的血清 Hcy、TC、TG、LDL-C、HDL-C。

1.3.2 **评定标准** (1)肾功能:根据 CysC 结果,采用罗氏诊断公司 Egfr Grubb 方程式,eGFR (mL/min·1.73 m^2)=84.69×[CysC(mg/L)]-1.680 计算肾小球滤过率(eGFR)[12],肾功能评价参考《基于血清胱抑素 C 的肾功能估计公式在肾功能评价中的价值》[13];(2)血脂项目评价:参考《中国成人血脂异常防治指南》(2016 年修订版)[14]。

1.4 统计学方法

所有资料均采用 SPSS17.0 软件进行统计分析。对采用 Kolmogorov-Smironv 检验对数据进行正态性检验,若符合正态分布,计量资料应用平均值± 标准($\bar{x}\pm s$)表示,的两组间比较采用 t 检验;多组间率的比较采用 x^2 检验,采用 Spearman 相关分析,探讨肾功能下降的血脂异常因素,采用多元 Logistic 回归分析, 因变量:eGFR<60 mL/min·1.73 m^2, 血清 Hcy、TG、TC、HDL-C、LDL-C 进行逐步回归分析。P<0.05 为差异有统计学意义。

2 结果

2.1 观察组与对照组 Hcy、血脂指标的比较

观察组患者的血清 Hcy、TC、TG、HDL-C、LDL-C 水平均明显高于对照组,差异具有统计学意义(P<0.05),见表 1。

表 1 观察组与对照组 Hcy、血脂指标的比较($\bar{x}\pm s$)

Table 1 Comparison of Hcy and blood lipid indexes between observation group and control group($\bar{x}\pm s$)

Groups	N	TC(mmol/L)	TG(mmol/L)	HDL-C(mmol/L)	LDL-C(mmol/L)	Hcy(μmol/L)
Control group	100	4.04± 1.34	1.21± 0.56	1.18± 0.91	2.77± 0.44	9.93± 2.32
Observation group	300	7.08± 1.07'	1.74± 0.73'	1.76± 1.02'	3.64± 1.27'	16.65± 2.94'

注:与对照组比较,' P<0.05。

Note: Compared with control group,' P<0.05.

2.2 Hcy 正常组与 Hcy 异常组血脂指标的水平比较

Hcy 异常组血清 LDL-C 水平明显高于 Hcy 正常组 (P<0.05),HDL-C 水平明显低于 Hcy 正常组 (P<0.05);Hcy 正常组与 Hcy 异常组 TG、TC 比较, 差异均无统计学意义 (P>0.05),见表 2。

表 2 观察组 Hcy 正常组与 Hcy 异常组血脂指标的水平比较($\bar{x}\pm s$)

Table 2 Blood lipid levels of Hcy normal group and Hcy abnormal group

Groups	N	TC(mmol/L)	TG(mmol/L)	HDL-C(mmol/L)	LDL-C(mmol/L)
Hcy normal group	167	6.79± 2.21	1.77± 0.65	1.96± 0.35	3.27± 0.37
Hcy exception group	133	7.27± 2.15	1.63± 0.78	1.28± 0.11*	3.92± 1.21*

注:与正常组比较,P>0.05。与对照组比较,* P<0.05。

Note: Compared with the Hcy normal group, P>0.05. Compared with the control group, * P<0.05.

2.3 观察组血清 Hcy 与 eGFR 值、血脂指标水平的相关性分析

观察组患者血清 Hcy 与 eGFR、HDL-C 水平呈负相关关系(r=-0.573、-0.414,P<0.05);与 TG 水平呈正相关(r=0.432,P<0.05),与 TC、LDL-C 不相关(P=0.527、0.121)。

2.4 观察组肾移植术后 eGFR 下降的影响因素分析

通过 Logistic 回归分析,Hcy、TG、LDL-C 水平均与患者 eGFR 下降有关(P<0.05),见表 3。

表 3 观察组肾移植术后 eGFR 下降因素 Logistic 回归分析

Table 3 Logistic regression analysis of eGFR decrease factors after renal transplantation in observation group

Risk factors	β	SE	Wald x^2	P	OR(95%CI)
TG	0.686	0.225	9.321	0.002	1.038~4.284
LDL	1.184	0.539	4.821	0.028	1.216~3.941
Hcy	0.054	0.020	7.443	0.001	1.437~2.123

3 讨论

慢性肾衰竭是慢性肾脏病进展过程中的终末阶段,肾脏替代治疗是治疗慢性肾衰唯一有效的治疗手段,其包括:腹膜透析、血液透析、肾移植。随着器官移植技术的不断发展,移植肾的存活率不断提高,使肾移植术成为最有效的肾脏替代治疗手段[15-17]。DGF 是影响肾移植近期及远期效果的重要因素,是肾移植术后发生急性肾功能衰竭的一种形式,其原因包括[18-20]:① 肾性因素:移植肾的排斥反应、急性肾小管坏死、药物中毒等;② 肾前性因素:移植肾动脉狭窄、血管栓塞、血液灌流不足等;③ 肾后性因素:尿路梗阻。肾血流减少、肾小球滤过率降低等因素可以引起肾组织缺氧,诱发细胞因子激活、活性氮氧化物、超氧化物及凝血系统的激活,最终导致肾组织细胞死亡、肾功能损伤。

在本次研究中,观察组患者检测的 Hcy、TC、TG、HDL-C、LDL-C 均明显高于对照组,差异具有统计学意义(P<0.05),这说明与健康人群比较,慢性肾衰患者在肾移植术后血脂、Hcy 水平均显著升高。我们认为可能是在肾移植手术时机体产生的应激反应和术后的排异反应引起血脂异常,再者患者服用环孢素 A、雷帕霉素等抗排异药物也可引起机体代谢异常,导致血脂水平上升;同时术后患者肾功能受损可导致尿蛋白排泄量过高,易引起继发性血脂异常,且肾功能受损后可导致亚甲基四氢叶酸还原酶、甲基转移酶缺乏或活性下降,Hcy 不能及时清除,导致 Hcy 水平上升[21,22]。同时本研究还显示,观察组 Hcy 异常组血清 LDL-C 水平明显高于 Hcy 正常组,HDL-C 水平明显低于 Hcy 正常组,且观察组患者血清 Hcy 与 eGFR、HDL-C 水平呈负相关,与 TG 水平呈正相关。这说明 Hcy 异常可引起 LDL-C 水平升高,HDL-C 水平降低,同时进一步说明 Hcy 水平与肾功能存在联系。这主要是 Hcy 可以促进动脉平滑肌细胞增生,增加氧化型的 LDL-C 水平,降低 HDL-C 的作用,同时 Hcy 可以通过影响肾功能来影响血脂的正常代谢[23-24]。通过 Logistic 回归分析,Hcy、TG、LDL-C 水平均与患者 eGFR 下降有关。高 Hcy 血症可对肾脏血管的内皮细胞造成损伤,同时增加肾小球机械屏障以及电荷屏障的损伤程度,增加肾小球囊内压,损伤肾功能,而肾功能受损又会进一步造成 Hcy 水平上升,形成恶性循环[25,26]。TG、LDL-C 水平过高会增加血液粘稠度,导致肾脏血管病变,而 LDL-C 水平升高可引起动脉平滑肌细胞增生,促进动脉粥样硬化,增加肾脏血管的内压,使得肾小球的滤过性增强,同时 LDL-C 水平升高还可以促进肾间质纤维化,损伤肾功能[27,28]。由此可见,血脂异常和高 Hcy 血症均可导致肾功能受损,慢性肾衰患者在肾移植术后应对其血脂指标和 Hcy 进行监测,若发现血脂异常可服用他汀类药物进行调脂,发现 Hcy 过高可通过补充叶酸或维生素 B12 来调节其水平,以减少对肾功能的损伤[29,30]。

综上所述,慢性肾衰患者在肾移植术后会出现血脂、Hcy 水平上升,同时肾功能降低。Hcy、TG、LDL-C 水平均与患者 eGFR 下降有关,临床上可对上述指标进行监测,发现异常及时处理,减少肾功能受损情况。

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