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◇临床医学◇

基于全身免疫炎症指数和预后营养指数的列线图模型 在肝移植术后急性肾损伤的预测价值探讨

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摘要 目的 探讨原位肝移植(orthotopic liver transplantation, OLT)术后发生急性肾损伤(acute kidney injury, AKI)的独立危险因素,并构建列线图预测模型以个性化预测AKI事件的发生。**方法** 回顾性分析2017年3月至2021年3月于中国人民解放军东部战区总医院行OLT手术的终末期肝病病人作为研究对象。入组病人根据OLT术后7 d内是否发生AKI事件分为两组。采用单因素、多因素logistic回归模型分析AKI的独立危险因素。多因素筛选出的独立危险因素进一步通过R软件绘制列线图预测模型并评估。**结果** 本研究共纳入237例OLT手术病人,其中101例病人术后7 d内发生了AKI,发生率为42.6%。AKI组病人的术前伴随的肝昏迷比例[22.8%(23/101)比9.6%(13/136)]、APACHE II评分、手术时间[(7.7±1.8)h比(7.0±1.6)h]、术中出血量[(3 002±1 606)mL]比(2 525±1 383)mL]、红细胞输注量、术前总胆红素、国际标准化比值(international normalized ratio, INR)(1.74±0.26比1.63±0.23)、肌酐及全身免疫炎症指数(systemic immune-inflammation index, SII)(725±458比553±355)水平均显著高于非AKI组($P < 0.05$),而预后营养指数(prognostic nutritional index, PNI)(41.4±5.3比45.0±6.1)则显著低于非AKI组病人($P < 0.05$)。多因素logistic回归分析提示PNI[OR 95%CI: 2.63(1.67, 3.87), $P = 0.005$]、SII[OR 95%CI: 2.65(1.18, 4.41), $P = 0.011$]、INR[OR 95%CI: 1.73(1.02, 3.01), $P = 0.017$]、出血量[OR 95%CI: 2.26(1.16, 4.33), $P = 0.014$]、肝昏迷[OR 95%CI: 2.51(1.19, 5.21), $P = 0.015$]是术后7 d发生AKI事件的独立危险因素。根据这5个危险因素构建的列线图风险模型对于肝移植病人术后AKI发生预测价值较好,受试者操作特征(ROC)曲线下面积为0.73[95%CI: (0.65, 0.81)]。**结论** 基于SII、PNI等因素构建的风险模型可有效预测OLT病人术后AKI事件的发生。

关键词 肝移植; 手术后并发症; 移植受体; 急性肾损伤; 列线图; 预后营养指数; 全身免疫炎症指数

Exploring the predictive value of a nomogram model based on the SII and PNI score for acute kidney injury after orthotopic liver transplantation

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Abstract Objective To investigate the independent risk factors for acute kidney injury (AKI) after orthotopic liver transplantation (OLT) and to construct a nomogram prediction model to predict AKI events. **Methods** Patients with end-stage liver disease who underwent OLT surgery from March 2017 to March 2021 in the Department of Anesthesiology, General Hospital of Eastern Theater Command of PLA were retrospectively analyzed as study subjects. The enrolled patients were divided into two groups according to whether AKI occurred within 7 days after OLT. Univariate and multivariate logistic regression models were used to analyze the independent risk factors for AKI. The screened independent risk factors screened by multiple factors were further predicted by the nomogram prediction model and evaluated by R software. **Results** A total of 237 OLT patients were enrolled in this study, of whom 101 patients developed AKI within 7 days after surgery, with an incidence of 42.6%. The proportion of preoperative hepatic encephalopathy [22.8% (23/101) vs. 9.6% (13/136)], APACHE II score, surgery duration [(7.7±1.8) vs. (7.0±1.6) h], intraoperative hemorrhage [(3 002±1 606) vs. (2 525±1 383) mL], erythrocyte transfusion, preoperative total bilirubin, international normalized ratio (INR) (1.74±0.26 vs. 1.63±0.23), creatinine, and systemic immune-inflammation index (SII) (725±458 vs. 553±355) levels were significantly higher in the AKI group than that in the non-AKI group ($P < 0.05$), while the prognostic nutritional index (PNI) (41.4±5.3 vs. 45.0±6.1) was significantly lower than that in the non-AKI group ($P < 0.05$). The multivariate logistic regression analysis suggested that PNI [OR 95%CI: 2.63 (1.67, 3.87), $P = 0.005$], SII [OR 95%CI: 2.65 (1.18, 4.41), $P = 0.011$], INR [OR 95%CI: 1.73 (1.02, 3.01), $P = 0.017$], bleeding [OR 95%CI: 2.26 (1.16, 4.33), $P = 0.014$], and hepatic coma [OR 95%CI: 2.51 (1.19, 5.21), $P = 0.015$] were the independent risk factors for the occurrence of an AKI event at 7 d postoperatively. The nomogram risk model constructed based on these 5 risk factors had a good predictive value for

the occurrence of postoperative AKI in OLT patients, with an area under the receiver operating characteristic (ROC) curve of 0.73 [95%CI:(0.65,0.81)]. **Conclusion** The nomogram risk model constructed based on the SII, PNI and other factors can effectively predict the occurrence of postoperative AKI events in OLT patients.

Keywords Liver transplantation; Postoperative complications; Transplant recipients; Acute kidney injury; Nomogram; Prognostic nutritional index; Systemic immune-inflammation index

原位肝移植(orthotopic liver transplantation, OLT)手术是终末期肝病病人的最主要的治疗策略。近年来,随着器官保存、手术及围术期管理技术及水平的发展,肝移植受者总体生存率有了较大的改善。但肝移植术后常会发生各种急性、慢性并发症,严重影响了病人预后^[1]。其中,急性肾损伤(acute kidney injury, AKI)是肝移植术后常见的并发症,研究指出术后AKI在OLT受者中的发生率可达50%以上,可致病人术后住院时间延长、死亡率增加^[2]。目前国内外尚还缺乏及时有效的预测因素,故而,本研究即旨在寻找术后AKI事件的独立危险因素,建立列线图预测模型,以期个体化预测术后AKI事件的发生,从而改善病人预后。

1 资料与方法

1.1 一般资料 本研究回顾性选取2017年3月至2021年3月237例于中国人民解放军东部战区总医院行原位肝移植手术的终末期肝病病人作为研究对象。纳入标准:(1)年龄范围18~65周岁;(2)拟接受OLT手术的终末期肝病病人;(3)麻醉、手术及围术期管理均由同一治疗或麻醉小组完成;(4)术后接收免疫抑制治疗。排除标准:(1)术前即伴有肾功能障碍,或其他脏器功能严重障碍者;(2)既往有器官移植术史者;(3)联合脏器移植者;(4)临床资料不完整者。本研究获中国人民解放军东部战区总医院行伦理委员会批准,病人或近亲属对研究方案签署知情同意书。

1.2 研究方法 入组病人根据OLT术后7 d内是否发生AKI事件分为两组。目前AKI尚缺乏国际统一诊断标准,本研究采用应用广泛、较为公认的全球改善肾脏病预后组织(kidney disease improving global outcomes, KDIGO)制定的AKI诊断指南^[3]:①48 h内血清肌酐(serum creatinine, Scr)升高 $\geq 26.5 \mu\text{mol/L}$ (0.3 mg/dL);②术后7 d内Scr升高超过基线值 ≥ 1.5 倍;③尿量减少, $< 0.5 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$,且持续 $> 6 \text{ h}$ 。符合以上3个指标中的一项即可诊断AKI。

收集、观察及分析指标如下:(1)基线资料:包括性别、年龄、身体质量指数(body mass index, BMI)、并存疾病、病因及术前并发症;(2)临床及治疗相关指标:包括急性生理和慢性健康(acute physiology and chronic health evaluation, APACHE) II 评

分、终末期肝病(model for end-stage liver disease, MELD)评分、Child评分、手术方式、术中药物、手术时间、出血量及输血;(3)术前血液指标:包括谷丙转氨酶(alanine transaminase, ALT)、谷草转氨酶(aspartate aminotransferase, AST)、总胆红素、国际标准化比值(international normalized ratio, INR)、肌酐、白蛋白(albumin, Alb)、淋巴细胞(lymphocyte, L)、中性粒细胞(neutrophil, N)、血小板(platelet, Plt)等。

依据既往报道^[4],预后营养指数(prognostic nutritional index, PNI)计算公式: $\text{PNI} = \text{Alb}(\text{g/L}) + 5 \times \text{L}(\times 10^9/\text{L})$;全身免疫炎症指数(systemic immune-inflammation index, SII)计算公式: $\text{SII} = \text{Plt} \times \text{N} / \text{L}(\times 10^9/\text{L})$ 。

1.3 统计学方法 采用SPSS 19.0、Graphpad 8.0及R(4.0.2)进行统计分析,方法采用 χ^2 、 t 检验。连续性变量对复发的预测价值及临界值采用受试者操作特征(receiver operator characteristic, ROC)曲线分析。复发的独立危险因素采用单因素、多因素logistic回归分析。多因素筛选出的独立危险因素进一步通过R软件绘制列线图预测模型,并评估该模型预测效果。 $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 基线指标 依据纳入、排除标准,本研究共纳入237例OLT手术病人,其中101例病人术后7 d内发生了AKI,发生率为42.6%(101/237)。两组病人基线资料详见表1,可见AKI组病人的术前伴随的肝昏迷比例显著高于非AKI组病人($P = 0.005$),其余基线资料均差异无统计学意义($P > 0.05$)。

2.2 临床及治疗指标 两组病人的临床及治疗相关指标结果提示AKI组病人APACHE II评分、手术时间、术中出血量、红细胞输注量均显著高于非AKI组病人($P < 0.05$),其余指标均差异无统计学意义($P > 0.05$)。见表2。

2.3 血液指标 两组病人术前血液学相关指标详见表3,结果提示AKI组病人术前总胆红素、INR、肌酐及SII水平均显著高于非AKI组($P < 0.05$),而PNI则显著低于非AKI组病人($P < 0.05$),其余指标差异无统计学意义($P > 0.05$)。

2.4 AKI的危险因素分析 将表1~3中 $P < 0.05$ 的变量纳入单因素logistic回归分析模型中,随后将 $P <$

表1 OLT手术病人237例临床指标比较

指标	术后7 d AKI发生		$\chi^2(t)$ 值	P值
	是(n=101)	否(n=136)		
性别/例			0.69	0.405
男	74	106		
女	27	30		
年龄/(岁, $\bar{x} \pm s$)	45.7±6.9	44.2±7.7	(1.55)	0.123
BMI/(kg/m ² , $\bar{x} \pm s$)	22.9±2.7	23.1±2.9	(0.54)	0.589
并存疾病/例				
糖尿病	13	11	1.46	0.227
高血压	18	15	2.23	0.135
冠心病	8	10	0.03	0.870
病因/例			1.50	0.682
肝癌	56	69		
肝硬化	30	40		
肝硬化合并肝癌	9	19		
其他	6	8		
术前并发症/例				
腹水	72	85	2.00	0.157
肺部感染	11	10	0.90	0.343
上消化道出血	21	26	0.10	0.749
肝昏迷	23	13	7.86	0.005

注:OLT为原位肝移植,AKI为急性肾损伤,BMI为身体质量指数。

0.05的7个因素继续纳入多因素 logistic 回归模型中, PNI[OR 95%CI: 2.63 (1.67, 3.87), P=0.005]、SII [OR 95%CI: 2.65 (1.18, 4.41), P=0.011]、INR [OR 95%CI: 1.73 (1.02, 3.01), P=0.017]、出血量 [OR 95%CI: 2.26 (1.16, 4.33), P=0.014]、肝昏迷 [OR 95%CI: 2.51 (1.19, 5.21), P=0.015]是术后7 d发生AKI事件的独立危险因素。

2.5 连续性变量对AKI的预测价值 多因素 logistic 回归分析中P<0.05的连续性变量包括INR、PNI、SII和术中出血量。ROC曲线分析结果提示这4个因素均为术后AKI的预测因子(均P<0.05),曲线下面积(area under the curve, AUC)分别为0.66、0.68、0.60、0.58,临界值分别为1.70、44.15、669.50和2 495.00。

2.6 AKI列线图预测模型建立及评估 我们将多

表3 OLT手术病人237例血液指标比较/ $\bar{x} \pm s$

指标	术后7 d AKI发生		t值	P值
	是(n=101)	否(n=136)		
ALT/(U/L)	104.3±35.3	96.3±31.7	1.83	0.069
AST/(U/L)	112.7±41.6	103.8±35.9	1.76	0.079
总胆红素/(μ mol/L)	173.3±76.4	153.3±66.7	2.14	0.033
INR	1.74±0.26	1.63±0.23	3.44	0.001
肌酐/(μ mol/L)	76.4±9.8	72.2±10.1	3.21	0.002
SII	725±458	553±355	3.26	0.001
PNI	41.4±5.3	45.0±6.1	4.75	<0.001

注:OLT为原位肝移植,AKI为急性肾损伤,ALT为丙氨酸转氨酶,AST为天冬氨酸转氨酶,INR为国际标准化比值,SII为全身免疫炎症指数,PNI为预后营养指数。

因素分析结果得出的5个独立危险因素进一步纳入预测模型,采用R绘制列线图模型(图1),该模型可个体化预测肝移植病人术后AKI发生概率。

3 讨论

肝移植是终末期肝病的最佳治疗策略,而术后AKI是肝移植术后常见的并发症,严重影响了预后^[5]。本研究中入组病人术后7d内AKI事件发生率为42.6%,与Durand等^[6]报道的50%相近,低于张颖颖等^[7]报道的57.4%,而显著高于Park等^[8]报道的23.1%。不同研究所报道的AKI发生率差别较大,我们考虑原因可能包括AKI诊断标准差异、病人特征、手术类型、手术操作、围术期管理等差异,尤其是目前国际上还缺乏AKI的诊断金标准可能是最主要原因。

通过因素筛选、进一步单因素及多因素 logistic 回归分析,本研究最终确定了,PNI、SII、INR、出血量及肝昏迷是术后AKI事件的5个独立危险因素。Zongyi等^[9]的一项多中心回归性研究指出肝移植术中出血量、红细胞输注量的增加与术后AKI的发生关系密切,与本研究结果相一致。Catalán等^[10]的一项长期、单中心、前瞻性的研究指出肝移植术前肝性脑病的存在可强烈预测术后AKI事件的发生,这与本研究结论相一致。另外,Silver等^[11]针对青少年

表2 OLT手术病人237例临床及治疗指标比较

指标	术后7 d AKI发生		$t(\chi^2)$ 值	P值	指标	术后7 d AKI发生		$t(\chi^2)$ 值	P值
	是(n=101)	否(n=136)				是(n=101)	否(n=136)		
APACHE II评分/(分, $\bar{x} \pm s$)	11.5±1.8	11.1±1.6	2.26	0.025	术中药物				
MELD评分/(分, $\bar{x} \pm s$)	20.1±6.5	19.2±5.8	1.12	0.263	甘露醇/(mL, $\bar{x} \pm s$)	304±185	276±154	1.27	0.206
Child评分/(分, $\bar{x} \pm s$)	10.1±1.8	9.9±2.0	0.79	0.428	碳酸氢钠/(mL, $\bar{x} \pm s$)	378±255	352±242	0.80	0.425
手术方式/例			(2.45)	0.294	胶体/(mL, $\bar{x} \pm s$)	980±504	864±490	1.78	0.064
经典非转流	50	81			手术时间/(h, $\bar{x} \pm s$)	7.7±1.8	7.0±1.6	3.16	0.002
背驮式	41	43			出血量/(mL, $\bar{x} \pm s$)	3 002±1 606	2 525±1 383	2.45	0.015
其他	10	12			红细胞输注/(mL, $\bar{x} \pm s$)	2 980±2 113	2 365±1 645	2.52	0.012
术中使用肾上腺素者/例	30	35	(0.46)	0.498	血浆输注/(mL, $\bar{x} \pm s$)	1 630±632	1 480±553	1.94	0.053

注:OLT为原位肝移植,AKI为急性肾损伤,APACHE为急性生理和慢性健康评分,MELD为终末期肝病评分。

注: AKI为急性肾损伤, INR为国际标准化比值, SII为全身免疫炎症指数, PNI为预后营养指数。

图1 肝移植病人术后AKI预测因素列线图风险模型

肝移植病人的单中心研究指出,术前INR水平与术后AKI发生密切相关,术前INR每增加一个单位相对应的AKI发生风险均明显增高。本研究结果也提示INR是术后AKI发生的独立危险因素,这与上述研究结果相一致。此外,还有研究SII指数能够作为肝癌术后AKI发生^[12]或急性胰腺炎病人并发AKI^[13]的预测因子。Min等^[14]研究发现改良PNI指数能够作为肝移植术后AKI的发生。Hu等^[15]指出PNI能够作为冠心病重症监护室病人发生AKI的预测因子。此外,PNI目前已被广泛应用于临床很多疾病的预后评估中^[16-17],如PNI能够应用于食管癌病人术后并发症及预后的评估^[18-19]。而本研究则首次报道SII、PNI指数均是肝移植病人术后AKI事件发生的独立危险因素。

此外,本研究根据多因素回归结果构建了列线图风险预测模型,模型评估结果提示该风险模型对于肝移植术后AKI事件的发生有着积极的预测价值。故而本研究根据PNI、SII指数等因素构建的列线图模型,可根据各项因素评分,从而个体化地预测肝移植病人术后发生AKI的风险,对于术后AKI事件的预防有着非常积极的应用价值。但本研究为单中心的回顾性研究,样本量有限,故而该预测模型还需进一步大样本的多中心研究来证实及优化。

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◇ 临床医学 ◇

抑郁症185例自杀意念、行为的危险因素分析

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摘要 目的 分析抑郁症病人自杀意念、行为的危险因素。**方法** 选取商丘市第二人民医院2020年1月至2021年8月185例抑郁症初诊病人(研究组),采用倾向值匹配法另选取185例健康志愿者(对照组)。采用聚合酶链式反应-限制性片段长度多态性(PCR-RFLP)检测两组脑源性神经营养因子(BDNF)基因多态性并比较;分别采用自杀意念自评量表(SIOSS)和专家访谈方式调查研究组的自杀意念、行为,采用logistic多元回归法分析自杀意念、行为的影响因素。**结果** 两组BDNF第66个氨基酸处的缬氨酸突变为蛋氨酸(Val66Met)基因型分布与等位基因频率比较差异无统计学意义($P>0.05$),且均符合遗传平衡规律($P>0.05$);研究组离婚/丧偶病人SIOSS评分高于未婚、已婚[(12.86±3.05)分比(8.73±1.98)分、(10.02±2.01)分]($P<0.05$),无业病人SIOSS评分高于在编人员、普通职员/个体户[(13.63±3.04)分比(8.04±1.95)分、(9.78±2.04)分]($P<0.05$),收入水平<3 000元/月SIOSS评分高于3 000~5 000元、>5 000元/月[(13.12±3.08)分比(9.45±1.76)分、(8.10±1.52)分]($P<0.05$),独居、无家庭支持、无社会支持SIOSS评分均高于非独居、有家庭支持、有社会支持[(19.22±3.36)分比(8.12±1.88)分、(9.10±2.14)分比(14.09±2.35)分、(9.25±2.08)分比(12.17±2.44)分]($P<0.05$),BDNF Val66Met GG基因型SIOSS评分高于AA、AG基因型[(11.29±2.50)分比(7.65±1.77)分、(10.02±2.48)分]($P<0.05$);研究组有自杀意念占比44.32%(82/185),离婚/丧偶、无业、<3 000元/月、独居、无家庭支持、无社会支持、BDNF Val66Met GG基因型均是研究组有自杀意念的危险因素($OR=4.13, 4.74, 7.19, 6.06, 4.66, 4.75, 7.48, P<0.05$);研究组有自杀行为占比17.84%(33/185), <3 000元/月、无家庭支持、BDNF Val66Met GG基因型均是研究组有自杀行为的危险因素($OR=5.05, 3.41, 6.72, P<0.05$)。**结论** BDNF Val66Met GG基因型与抑郁症病人自杀意念、行为均有关。

关键词 抑郁症; 自杀意念; 自杀; 脑源性神经营养因子; 基因多态性; 危险因素

Risk factor analysis of suicidal ideation and behavior in patients with depression

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Abstract Objective To analyze the risk factors for suicidal ideation and behavior in patients with depression. **Methods** A total of 185 patients with depression initially diagnosed in the Second People's Hospital of Shangqiu City from January 2020 to August 2021 were selected (study group), and another 185 healthy volunteers were selected by propensity value matching (control group). Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to detect polymorphisms of the brain-derived neurotrophic factor (BDNF) gene in the two groups and compared them. Suicidal ideation and behavior of the study groups were investigated by using the Self-rating Idea of Suicide Scale (SIOSS) and expert interviews, respectively, and the influencing factors of suicidal ideation and behavior were analyzed by the logistic multiple regression method. **Results** There were no significant differences in the genotype distribution and allele frequency of valine mutated to methionine (Val66Met) at amino acid 66 of BDNF between the two groups ($P > 0.05$), and all of them were in accordance with the law of genetic equilibrium ($P > 0.05$). The SIOSS score of divorced/widowed patients in the study group was higher than that of unmarried and married patients [(12.86±3.05) scores vs. (8.73±1.98) scores, (10.02±2.01) scores] ($P < 0.05$). The SIOSS score of unemployed patients was higher than that of the workforce, ordinary employees/self-employed [(13.63±3.04) scores vs. (8.04±1.95) scores, (9.78±2.04) scores] ($P < 0.05$). The SIOSS scores were higher ($P < 0.05$) for income