·临床研究·

老年心脏手术患者术后急性肾损伤的发生率与预测因素研究

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【摘 要】 **目的** 调查老年心脏手术患者术后急性肾损伤(AKI)的发生率,分析其危险因素并探讨血清中性粒细胞明胶酶相关脂质运载蛋白(NGAL)的早期预测价值。**方法** 入选拟行择期心脏手术的患者(≥60岁)285例。根据AKI的发生情况将患者分为AKI组(n=81)及非AKI组(n=204)。分析术后2 h血清NGAL浓度对术后AKI的预测价值,筛选AKI的危险因素。**结果** 老年患者择期心脏术后AKI的发生率为28.4%(81/285)。术后2 h血清NGAL水平预测AKI的接受者操作特性(ROC)曲线下面积为0.622。多因素logistic回归分析筛选出术前合并慢性肾病、术中应用体外循环、围术期输注人工胶体量多、术后次日急性生理与慢性健康评分(APACHE)Ⅱ评分高和术后机械通气>24 h是术后AKI的危险因素。**结论** 老年患者心脏手术后AKI的发生率较高;术后早期血清NGAL预测AKI的作用有限;术前合并慢性肾病、术中应用体外循环、围术期输注人工胶体多、术后APACHE Ⅱ评分高和长时间机械通气伴随术后AKI风险增加。

【关键词】 老年人;心脏手术;急性肾损伤;危险因素;中性粒细胞明胶酶相关脂质运载蛋白

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Incidence and predictive factors of acute kidney injury in elderly patients after cardiac surgery

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【**Abstract**】 **Objective** To investigate the incidence of acute kidney injury (AKI) in the elderly patients after cardiac surgery, and analyze risk factors and determine the early predictive value of serum neutrophil gelatinase-associated lipocalin (NGAL). **Methods** Two hundred and eighty-five elderly patients (≥ 60 years) who underwent elective cardiac surgery were recruited in this study. According to the occurrence of AKI or not, the patients were divided into AKI group (n = 81) and non-AKI group (n = 204). The predictive value of serum NGAL level in 2 h after surgery for AKI was evaluated with the area under receiver operating characteristic (ROC) curve. The risk factors of AKI were screened by logistic regression analysis. **Results** The incidence of postoperative AKI was 28.4% (81/285). The area under ROC curve of serum NGAL level in 2 h postoperatively for predicting AKI were 0.622. Multivariate logistic regression analysis identified that preoperative comorbidity of chronic kidney disease (CKD), intraoperative application of cardiopulmonary bypassing, perioperative infusion of large volume artificial colloids, high score of acute physiology and chronic health evaluation (APACHE) Ⅱ at the 1st day after surgery, and postoperative mechanical ventilation >24 h were independent risk factors for AKI. **Conclusion** The incidence of postoperative AKI remains high in the elderly patients after cardiac surgery. Early serum NGAL level has limited predictive value for the occurrence of AKI. Preoperative comorbidity of CKD, intraoperative application of cardiopulmonary bypassing, perioperative infusion of large volume artificial colloids, high APACHE Ⅱ score, and postoperative longtime mechanical ventilation increase the risk for AKI.

【**Key words**】 aged; cardiac surgery procedure; acute kidney injury; risk factors; serum neutrophil gelatinase-associated lipocalin

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急性肾损伤(acute kidney injury, AKI)是心脏手术后常见的并发症,发生率为 8.9% ~ 39.0%[1]。AKI 的发生增加了并发症的发生率和死亡率,即便轻微的肾功能损伤也与不良结局相关[2,3]。目前 AKI 的诊断主要依赖于血肌酐的变化,但这有一定的局限性:(1)血肌酐反映的是肾小球清除率,当肾小球损失 >50% 时才会出现明显变化;(2)血肌酐升高也可能是肾外原因所致;(3)血肌酐上升多出现于肾损伤后的 48 ~ 72 h。故采用血肌酐作为 AKI 早期诊断指标并不理想[4]。

中性粒细胞明胶酶相关脂质运载蛋白(neutrophil gelatinase-associated lipocalin, NGAL)是目前比较受关注的新型肾损伤标志物。尽管有不少研究观察了 NGAL 对心脏手术后 AKI 的预测效能,但结果差异较大[5-8]。本研究的目的是调查老年心脏手术患者术后 AKI 的发生情况,分析其预测因素,特别是术后早期血清 NGAL 对 AKI 的预测价值。

1 对象与方法

1.1 研究对象

本研究方案获北京大学第一医院及阜外心血管病医院医学伦理委员会批准(批准号分别是 2014 - 805 和 2015 - 646)。所有参研患者均由其本人或委托人签署知情同意书。

纳入患者 285 例。入选标准:(1)年龄≥60 岁;(2)拟接受择期冠状动脉搭桥和/或瓣膜置换手术。排除标准:术前接受肾脏替代治疗。根据 AKI 的发生情况将患者分为 AKI 组(n = 81)及非 AKI 组(n = 204)。

1.2 方法

术前收集人口学信息和基础资料,其中慢性肾病诊断采用改善全球肾脏病预后组织(Kidney Disease: Improving Global Outcomes, KDIGO)标准[9],即对健康有影响的肾脏结构或功能异常持续时间 >3 个月。麻醉前和术后 2 h 抽取血液标本测定血清 NGAL 浓度,采用 ELISA 法测定血清 NGAL 水平(检测由北京洛奇临床检验所有限公司完成)。术中收集麻醉、手术相关信息。术后前 5 d 每日随访患者,收集当日血肌酐和尿量信息;记录机械通气时间、ICU 停留时间和住院时间。术后 30 d 电话随访存活及再入院情况。

1.3 AKI 诊断标准及分期

采用 KDIGO 标准[10]将 AKI 分为 3 期。(1)1 期:血清肌酐水平上升至基线值的 1.5 ~ 1.9 倍或绝对值增加≥26.5 μmol/L,或尿量 <0.5 ml/(kg · h)持续 6 ~ 12 h;(2)2 期:血清肌酐水平上升至基线值的 2.0 ~ 2.9 倍,或尿量 <0.5 ml/(kg · h)持续时间≥12 h;(3)3 期:血清肌酐水平上升至基线值的 3 倍以上,或血肌酐值≥353.6 μmol/L,或开始肾脏替代治疗,或尿量 <0.3 ml/(kg · h)持续时间≥24 h,或无尿≥12 h。

1.4 统计学处理

采用 SPSS20.0 软件进行统计分析。计量资料中呈正态分布者采用均数 ± 标准差($\bar{x} \pm s$)表示,两组间比较采用 t 检验;呈偏态分布者以中位数(M)和四分位数间距(Q)分别表示数据的集中趋势和离散趋势,两组间比较采用秩和检验。计数资料以百分率表示,两组间比较采用 χ^2 检验。采用受试者工作特征(receiver operating characteristic, ROC)曲线下面积评价 NGAL 对 AKI 的预测能力。采用logistic 回归分析筛选发生 AKI 的危险因素。P <0.05 为差异具有统计学意义。

2 结 果

2.1 两组患者基线资料比较

与非 AKI 组患者相比,AKI 组患者的年龄更大、合并高脂血症更多、使用利尿剂比例更高、欧洲心血管手术危险因素评分系统(European system for cardiac operative risk evaluation, EuroSCORE)分值也更高,且差异均具有统计学意义(P <0.05;表 1)。

2.2 两组患者术后 AKI 及围术期情况比较

285 例患者中,共有 81 例(28.4%)出现 AKI,其中 1 期 71 例(87.6%)、2 期 7 例(8.7%)、3 期 3 例(3.7%)。术后每日新发 AKI 病例情况如图 1 所示,表明术后前 2d 新发病例数占全部 AKI 例数的 95.1%,其中术后第 1 天为高峰时期,新发病例占全部 AKI 例数的 77.8%。

与非 AKI 组患者相比,AKI 组患者接受瓣膜置换或联合手术更多、体外循环使用比例更高、主动脉阻断时间更长、麻醉和手术时间更长、输注人工胶体液和血液制品更多、术后 APACHE Ⅱ评分更高、使用 IABP 比例更高、术后低血压发生率更高、使用多巴胺剂量更大、机械通气时间也更长,差异均具有统计学意义(P <0.05;表 2)。

2.3 两组患者术后 NGAL 水平比较及其对术后 AKI 的预测价值

13 例患者缺乏术后 2 h 血清标本,故共有 272 例患者资料用于术后 2 h NGAL 对 AKI 的预测

表1 基线资料比较

Table 1 Comparison of baseline data between two groups

Item	AKI group (n=81)	Non-AKI group (n=204)	P value
Age(years, $\bar{x}\pm s$)	67.9±5.5	66.5±5.3	0.046
Male[n(%)]	55(67.9)	142(69.6)	0.778
BMI(kg/m^2, $\bar{x}\pm s$)	24.9±3.1	25.2±3.1	0.515
Comorbiditiy[n(%)]			
Hypertension	49(60.5)	131(64.2)	0.557
Diabetes mellitus	28(34.6)	64(31.4)	0.603
Stroke	16(19.8)	43(21.1)	0.872
Hyperlipemia	36(44.4)	63(30.9)	0.030
Chronic kidney disease	5(6.2)	3(1.5)	0.077
Acute myocardial infarction before surgery	6(7.4)	22(10.8)	0.388
Charlson comorbidity index[M(Q_1, Q_3)]	1(0, 1)	0(0, 1)	0.257
NYHA function class[n(%)]			0.879
1	1(1.3)	3(1.7)	
2	50(66.7)	129(70.9)	
3	22(29.3)	47(25.8)	
4	2(2.7)	3(1.6)	
Drug regularly administrated before hospitalization[n(%)]			
CCB	23(28.4)	55(27.0)	0.807
β-receptor antagonist	36(44.4)	93(45.6)	0.861
ACEI/ARB	29(35.8)	67(32.8)	0.634
Statins	35(43.2)	103(50.5)	0.267
Diuretics	20(24.7)	24(11.8)	0.006
Antiplatelet drugs	44(54.3)	123(60.3)	0.356
ASA class[n(%)]			0.663
2	1(1.2)	2(1.0)	
3	71(87.7)	186(91.2)	
4	9(11.1)	16(7.8)	
EuroSCORE score[M(Q_1, Q_3)]	3(2, 5)	3(2, 5)	0.039
Laboratory index before surgery[M(Q_1, Q_3)]			
NGAL(ng/ml)	84.8(69.8, 124.7)	89.6(64.9, 121.7)	0.831
Serum creatinine(μmol/L)	83.0(72.3, 100.0)	86.0(74.1, 98.5)	0.877
Serum urea(mmol/L)	5.8(4.8, 7.2)	5.6(4.7, 7.3)	0.307

BMI: body mass index; NYHA: New York Heart Association; CCB: calcium channel blocker; ACEI/ARB: angiotensin converting enzyme inhibitor/angiotensin receptor blocker; EuroSCORE: European System for Cardiac Operative Risk Evaluation; NGAL: neutrophil gelatinase-associated lipocalin

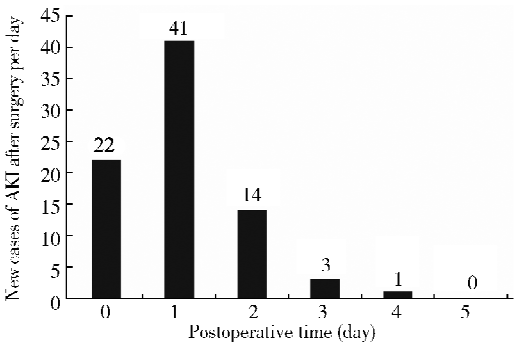


图1 术后急性肾损伤每日新发病例数

Figure 1 New cases of AKI after surgery per day

AKI: acute kidney injury

效能分析。AKI组患者(n=77)术后2 h血清NGAL水平显著高于非AKI组患者(n=195),差异具有统计学意义[181.9(124.2, 280.9) *vs* 133.2(74.5,225.7),P=0.002]。以术后2 h血清NGAL水平及是否发生AKI做ROC曲线,得出其预测AKI的效能为0.622(95% CI:0.551~0.693);截断值为123 ng/ml时,灵敏度和特异度分别为77%和46%(图2)。

2.4 两组患者术后实验室指标及住院情况比较

AKI组患者术后5 d内血肌酐和血尿素氮水平的峰值均显著高于非AKI组,且AKI组患者的ICU停留时间也更长,差异均具统计学意义(P<0.05;表3)。

2.5 术后AKI的危险因素分析

以P<0.10为标准,采用单因素logistic回归分析并经共线性检验,共16项变量进入多因素logistic回归分析(逐步后退法)。结果显示术前合并慢性肾

表2 两组患者围手术期情况比较

Table 2 Comparison of conditions during perioperative period between two groups

Item	AKI group (n=81)	Non-AKI group (n=204)	P value
Surgery[n(%)]			0.002
CABG	46(56.8)	158(77.5)	
Valve replacement	18(22.2)	24(11.8)	
CABG and valve replacement	17(21.0)	22(10.8)	
CPB use[n(%)]	55(67.9)	66(32.4)	<0.001
Anesthesia duration[min, M(Q_1, Q_3)]	280(230, 342)	246(215, 282)	<0.001
CPB time[min, M(Q_1, Q_3)]	110(85, 145)	99(77, 122)	0.079
Aortic cross clamping time[min, M(Q_1, Q_3)]	84(63, 102)	68(57, 88)	0.026
Surgery duration[min, M(Q_1, Q_3)]	218(176, 274)	175(153, 210)	<0.001
Special fluid infusion[ml, M(Q_1, Q_3)]*			
Artificial colloid	2250(1300, 2900)	1500(500, 2500)	0.001
Mannitol	250(125, 250)	250(125, 250)	0.684
Homologous red cell blood transfusion	800(400, 1200)	400(400, 800)	0.003
Fresh frozen plasma	800(400, 1200)	400(400, 800)	<0.001
Intraoperative hypotension[n(%)]#	9(11.1)	11(5.4)	0.089
APACHE Ⅱ[score, M(Q_1, Q_3)]△	10(8, 13)	7(6, 10)	<0.001
Postoperative hypotension[n(%)]#	13(16.1)	2(1.0)	<0.001
IABP use[n(%)]	12(14.8)	6(2.9)	<0.001
Total dose of dopamine[mg, M(Q_1, Q_3)]	720(388, 1299)	478(205, 848)	0.003
Mechanical ventilation time[h, M(Q_1, Q_3)]	17(14, 25)	13(7, 17)	<0.001
Dexmedetomidine infusion[n(%)]	37(45.7)	105(51.5)	0.378

*Indicate the total volume infused intraoperatively and during the first 5 days after surgery. #Decrease of systolic blood pressure of more than 30% from baseline for at least 15 min. △The worst score during the first 24 hours after surgery. CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; APACHE: acute physiology and chronic health evaluation; IABP: intra-aortic balloon pump

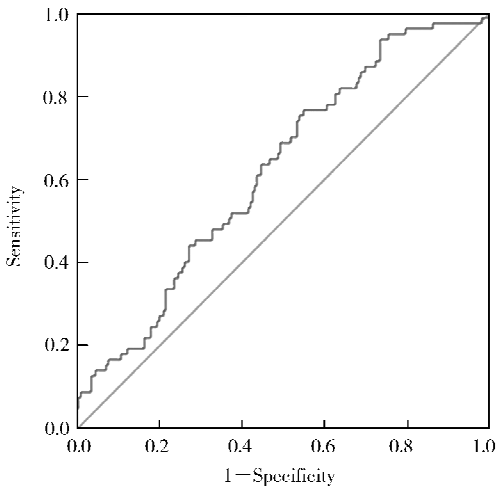


图2 术后2 h血清NGAL水平预测AKI的ROC曲线

Figure 2 ROC curve for assessment of the value of postoperative 2 h serum NAGL level in predicting AKI

NGAL: neutrophil gelatinase-associated lipocalin; AKI: acute kidney injury; ROC: receiver operating characteristic

病、术中应用体外循环、围术期输注胶体量多、术后第1天急性生理与慢性健康评分(acute physiology and chronic health evaluation, APACHE)Ⅱ评分高和术后机械通气时间>24 h是术后发生AKI的独立危险因素(表4)。

2.6 术后近期预后

术后随访30d,失访11例,共274例患者资料用于术后30d预后分析。随访结果显示,AKI组患者术后30d的全因死亡率显著高于非AKI组患者(P<0.05;表5)。

3 讨 论

本研究显示老年患者择期心脏术后,AKI的发生率为28.4%,这与文献报道的结果基本一致[1]。此外,本研究结果还显示AKI主要发生于术后早期,术后第1天为高峰时期,新发病例占全部AKI例数的77.8%。

在涉及AKI的早期诊断方面,NGAL是近年来受关注较多的生物标志物[11,12]。有些研究提示NGAL能很好地预测心脏手术后AKI的发生[7,8,13],但仍有争论[5,14]。Fanning等[6]的研究测定了术后18个时间点的血浆NGAL浓度,并未发现其能准确预测AKI的发生,大部分时间点检测值的曲线下面积波动在0.5~0.7之间。本研究也显示术后早期血清NGAL浓度对术后AKI的预测价值有限。这可能是由于血液中的NAGL部分来源于肝脏、肺脏以及其他非肾脏器官的上皮细胞[15],因而对肾损伤

表3 两组患者术后实验室指标及住院情况比较

Table 3 Comparison of postoperative laboratory indices and hospitalization between two groups [M(Q_1, Q_3)]

Item	AKI group (n=81)	Non-AKI group (n=204)	P value
Serum creatinine(μmol/L)	127.9(107.9, 157.1)	95.5(84.2, 106.0)	<0.001
Serum urea(mmol/L)	15.2(12.6, 20.0)	9.9(7.9, 12.5)	<0.001
Length of ICU stay(h)	66(36, 107)	45(29, 67)	0.002
Length of hospital stay(d)	17(14, 25)	19(14, 24)	0.616

表4 术后AKI危险因素logistic回归分析

Table 4 Logistic regression analysis of the risk factors for postoperative AKI

Item	Univariate analysis	Multivariate analysis		
	P value	OR	P value	95% CI
Age	0.048	–	–	–
Hyperlipemia	0.030	–	–	–
Chronic kidney disease	0.077	6.93	0.048	1.02–47.05
Diuretics regularly administrated before hospital	0.006	–	–	–
EuroSCORE	0.063	–	–	–
CABG surgery	0.002	–	–	–
CPB use	<0.001	4.14	<0.001	2.07–8.27
Surgery duration	<0.001	–	–	–
Intraoperative hypotension	0.088	–	–	–
Perioperative artificial colloid infusion	0.002	1.16	0.026	1.02–1.32
Perioperative homologous blood transfusion	0.004	–	–	–
Perioperative amount of dopamine	0.001	–	–	–
IABP use	<0.001	–	–	–
APACHE Ⅱ score of the first day after surgery	<0.001	1.30	<0.001	1.16–1.46
Mechanical ventilation >24 h	<0.001	4.16	0.015	1.32–13.10
Postoperative hypotension	<0.001	–	–	–

EuroSCORE: European System for Cardiac Operative Risk Evaluation; CABG: coronary artery bypass grafting; IABP: intra-aortic balloon pump; APACHE: acute physiology and chronic health evaluation

表5 两组患者预后情况比较

Table 5 Comparison of the outcome between two groups [n(%)]

Item	AKI group (n=80)	Non-AKI group (n=194)	P value
Readmission rate in 30 days after surgery	8(10.3)	23(11.8)	0.834
All-cause 30-day mortality	6(7.4)	0(0.0)	0.001

的预测价值有限。

本研究发现在校正了混杂因素后,术前合并慢性肾病、术中应用体外循环、围术期输注胶体量多、术后第1天APACHE Ⅱ评分高和术后机械通气时间>24 h是术后AKI发生的独立危险因素。术前合并慢性肾病[16]和术中使用体外循环[10]与术后AKI发生的关系已在其他研究中证实。尽管有争议,目前仍然认为人工胶体的使用与体外循环下心脏手术患者的AKI发生有关[17],本研究结果也证明这一点。

APACHE Ⅱ评分本身即涵盖了肌酐这一因素[18],本文结果提示病情危重的患者更容易发生AKI。机械通气会对肾脏产生不利影响,包括减少心排量、降低肾脏灌注以及激活交感肾素血管紧张素系统,从而导致肾脏滤过率下降[19]。此外,导致呼吸衰竭的原因可能也参与了AKI的发生[20]。本研究的结果与既往研究一致[21,22]。

与既往研究[23,24]有所不同的是,在校正混杂因素后本研究并未发现患者年龄与术后AKI的发生有关,这可能是由于我们入选的患者均为≥60岁的老年人;未发现围术期输注异体血与AKI的发生有关,尽管本研究的285例患者中有103例接受了围术期输血;亦未发现术前心功能差和术后低血压与AKI发生有关,这可能与本研究中纳入的相应病例数较少有关(术前心功能4级仅5例、术后低血压15例)。

本研究也存在一定局限性。我们入选的是年龄≥60岁的老年患者,也未包含其他手术类型如大血管、先心病矫治等,故研究结论的外推性受限制。

总之,本研究显示对于接受心脏手术的老年患者,术后AKI具有较高的发生率。术后早期血清

NGAL浓度对AKI的预测能力有限。术前合并慢性肾病、术中应用体外循环、围术期输注胶体量多、术后第1天APACHE Ⅱ评分高和术后机械通气时间>24 h是术后发生AKI的独立危险因素。术后发生AKI的患者ICU停留时间更长、术后30 d死亡率也更高。

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