·临床研究·

老年单纯急性肾损伤与 AonC 近期预后分析

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【摘 要】 **目的** 研究急性肾损伤(AKI)患者与慢性肾脏病(CKD)合并 AKI(AonC)患者的预后。**方法** 入选北京友谊医院医疗保健中心 2009 年 8 月至 2013 年 10 月期间收治的 AonC 患者 147 例,男性 105 例,女性 42 例,年龄(83.95±7.04)岁;同期单纯 AKI 患者 270 例,男性 226 例,女性 44 例,年龄(81.75±6.98)岁,比较两组患者近期(1 年内)预后。**结果** 单纯 AKI 患者随访 30 d 时的病死率高于 AonC 患者,差异有统计学意义($P<0.05$),随访 90 d 和 1 年时的病死率差异无统计学意义($P>0.05$);两组存活患者的肾功能恢复率差异无统计学意义($P>0.05$);不同估算肾小球滤过率(eGFR)水平的 AonC 患者随访 30 d、90 d 和 1 年病死率的差异无统计学意义($P>0.05$)。Cox 多因素回归分析表明是否合并 CKD 与患者 30 d 病死率无关($P=0.068$),与 AKI 分期、合并贫血、低蛋白血症、心力衰竭、恶性肿瘤和多器官功能障碍综合征(MODS)相关,肾脏替代治疗(RRT)为保护性因素。**结论** 老年 AKI 患者患病率和病死率高,是否合并 CKD 与近期预后无明显相关。

【关键词】 急性肾损伤;慢性肾脏病合并急性肾损伤;病死率;肾功能恢复
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Analysis of short-term prognosis between denovo-AKI and AonC in the elderly

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【**Abstract**】 **Objective** To analyze the prognosis of the elderly patients with acute kidney injury (AKI) and those suffering from acute on chronic kidney injury. **Methods** A total of 147 patients (105 males and 42 females, at a mean age of 83.95±7.04) with acute on chronic AKI (AonC) and 270 cases (226 males and 44 females, at a mean age of 81.75±6.98) with denovo AKI admitted in our center from August 2009 to October 2013 were enrolled in this study. Their short-term outcomes (within 1 year) were analyzed. **Results** The 30-day mortality was significantly higher in the AKI than the AonC patients ($P<0.05$), but there were no differences in that of 90-day and 1-year ($P>0.05$). No difference was seen in the recovery of renal function between the survivals from the 2 group ($P>0.05$). There were no differences in the 30-day, 90-day, 1-year mortalities among the AonC patients with different estimated glomerular filtration rates (eGFR). COX multivariate regression analysis showed that complication with chronic kidney disease (CKD) had no relation with the 30-day mortality ($P=0.068$), but is associated with AKI stage, anemia, hypoalbuminemia, heart failure, cancer, and multiple organ dysfunction syndrome (MODS). Renal replacement therapy was the protective factor for AonC patients. **Conclusion** The incidence and mortality of AKI were quite high in the AKI elderly patients. Complication of CKD is not related with their short-term prognosis.

【**Key words**】 acute kidney injury; acute on chronic kidney injury; mortality; recovery of renal function
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急性肾损伤(acute kidney injury,AKI)和慢性肾脏病(chronic kidney disease,CKD)是两个相互关联的临床综合征。流行病资料显示两个综合征之间的相互作用复杂,并且 CKD 合并 AKI(acute on chronic kidney disease,AonC)可能与 AKI 患者的预后不良相关[1],但也有研究表明基础肾功能不好可能与近期死亡率无关[2]。为了比较 AonC 和单纯 AKI 老年患者的预后,我们对北京友谊医院医疗保健中心老年患者的临床资料进行了回顾性分析。

1 对象与方法

1.1 研究对象

入选我院 2009 年 8 月至 2013 年 10 月期间 AonC 患者 147 例,男性 105 例,女性 42 例,年龄

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(83.95±7.04)岁;同期单纯AKI患者270例,男性226例,女性44例,年龄(81.75±6.98)岁。诊断符合改善全球肾脏病预后组织(Kidney Disease: Improving Global Outcomes, K/DIGO) 2012年诊断标准(不计尿量)。

AKI诊断标准[3]:48 h内血肌酐(serum creatinine, SCr)值升高≥26.5 μmol/L或≥基础值1.5倍,且明确或经推断上述情况发生在7 d内。Ⅰ期:SCr升高≥26.5 μmol/L或增至基础值的1.5~1.9倍;Ⅱ期:SCr升高至基础值的2.0~2.9倍;Ⅲ期:SCr升高≥353.6 μmol/L或增至基础值的3.0倍,或开始肾脏替代治疗(renal replacement therapy, RRT)。基础值为患者入院前6个月的SCr平均值;如平均值>住院期间发生AKI前SCr的最低值(非肾脏替代治疗)或入院前无SCr值记录,则住院期间发生AKI前的SCr最低值作为基础值。AKI恢复标准:脱离透析,SCr<基础值125%[1]。AonC诊断标准:应用2012年慢性肾脏病流行病学合作组(chronic kidney disease epidemiology collaboration, CKD-EPI)方程获得估算肾小球滤过率(estimated glomerular filtration rate, eGFR),基础eGFR<60 ml/(min·1.73 m^2)的AKI患者[1]。排除标准:无SCr值、单侧肾脏切除、规律透析患者。

1.2 方法

记录患者的年龄、性别、基础疾病、死亡时间以及AKI恢复时间;分析病因、死因、合并症、危险因素等临床特征;检测血SCr、血尿素氮(blood urea nitrogen, BUN)、血糖(glucose, Glu)、血红蛋白(hemoglobin, HB)和血白蛋白(albumin, Alb)等实验室指标;随访患者30 d、90 d、1年时的血SCr水平及是否死亡,分析死亡原因,随访截止时间为2014年6月。

1.3 统计学处理

应用SPSS19.0统计软件对数据进行分析。计量资料中呈正态分布者用均数±标准差($\bar{x}\pm s$)表示,两组比较采用t检验;呈偏态分布者用四分位间距[M(Q_1, Q_3)]表示,两组比较采用K-W秩和检验。计数资料用百分率表示,组间比较用χ^2检验。Cox回归分析死亡相关危险因素。以$P<0.05$为差异有统计学意义。

2 结 果

2.1 单纯AKI和AonC患者一般临床资料比较

两组患者病因差异无统计学意义($P>0.05$)。相比单纯AKI患者,AonC患者年龄偏大;SCr增加值较高,增加倍数低;BUN水平较高;AKI患者分期较低,Ⅰ期患者占55.1%;贫血和高血压患者比例较高,合并低蛋白血症及恶性肿瘤患者比例较低,差异有统计学意义($P<0.05$;表1)。

2.2 单纯AKI和AonC患者预后比较

队列研究要求随访率≥50%,一般为60%~80%[5]。本研究随访过程中两组均有失访患者,但失访率<15%且随访至30 d、90 d和1年时,两组失访率的差异无统计学意义($P>0.05$),故计算病死率时,将失访病例计为删失数据。单纯AKI患者随访30 d时的病死率高于AonC患者,差异有统计学意义($P<0.05$)。但随访90 d和1年时的病死率差异无统计学意义($P>0.05$;表2)。

2.3 单纯AKI与AonC患者肾功能恢复率比较

单纯AKI患者随访90d时存活96例,71例肾功能恢复,1年时存活78例,56例肾功能恢复。AonC患者随访90 d时存活60例,50例肾功能恢复,1年时存活45例,33例肾功能恢复,删除失访数据后比较两组存活患者的肾功能恢复率,两组差异无统计学意义($P>0.05$)。

2.4 单纯AKI与AonC患者30 d病死率危险因素分析

将既往研究与近期死亡可能的影响因素如AKI分期[4]、合并贫血[5]、低蛋白血症、心力衰竭、恶性肿瘤[6]、多器官功能障碍综合征(mutlipleorgan dysfunction syndrome, MODS)[7]、是否RRT[8]及是否合并CKD纳入Cox多因素回归方程进行分析。结果显示,是否合并CKD与患者30 d病死率无关($P=0.068$),与AKI分期、合并贫血、低蛋白血症、心力衰竭、恶性肿瘤和MODS相关,RRT为保护性因素($P<0.05$;表3)。

2.5 不同eGFR水平组AonC患者的病死率差异

AonC患者eGFR值60~45 ml/(min·1.73 m^2)有66例,eGFR值45~30 ml/(min·1.73 m^2)有41例,eGFR值30~15 ml/(min·1.73 m^2)有28例,eGFR<15 ml/(min·1.73 m^2)有12例。不同eGFR水平AonC患者随访30 d、90 d和1年病死率的差异无统计学意义($P>0.05$;表4)。

3 讨 论

机体随年龄增长发生的肾脏结构及功能变化,以及伴发的基础疾病可使老年人肾脏储备能力下降,对药物或毒素的代谢能力减退,从而对各种肾损伤因素的敏感性增高,易发生AKI。本研究中单纯AKI和AonC两组患者的病因差异无统计学意义,

依次为感染、低血容量、心功能不全和药物毒性作用等，与近期研究报道基本一致[11]。感染是老年AKI患者的首位病因[12]，主要为肺部感染，其中一部分可进展为脓毒血症[1]。年龄和营养不良与老年人免疫系统的低效应直接或间接相关，免疫功能低下使老年患者容易感染，并使AKI发生风险增加[11]。

表1 AonC和单纯AKI患者一般临床资料比较

Table 1 Comparison of clinical data between denovo AKI and AonC groups

Item	Denovo AKI group(n=270)	AonC group(n=147)	P value
Age(years, $\bar{x}\pm s$)	81.75±6.98	83.95±7.04	0.002
Male[n(%)]	226(83.7)	105(71.4)	0.003
Baseline eGFR[60 ml/(min·1.73 m^2), M(Q_1, Q_3)]	82.49(73.63,90.07)	42.79(28.50,52.37)	0.000
Baseline SCr[μmol/L, M(Q_1, Q_3)]	69.00(57.95,80.03)	120(106.00,171.00)	0.000
AKI SCr[μmol/L, M(Q_1, Q_3)]	131.50(112.00,153.50)	210.10(162.70,278.00)	0.000
Increased value of SCr[μmol/L, M(Q_1, Q_3)]	77.05(53.85,145.25)	111.0(59.90,219.00)	0.001
Increased fold of SCr	2.23(1.77,3.18)	1.80(1.40,2.50)	0.000
AKI BUN of disease[mmol/L, M(Q_1, Q_3)]	13.50(8.90,21.03)	18.13(12.54,26.44)	0.000
AKI stage[n(%)]			0.003
AKI Ⅰ	104(38.5)	81(55.1)	
AKI Ⅱ	89(32.8)	31(21.1)	
AKI Ⅲ	78(28.9)	34(23.2)	
Anemia[n(%)]	176(65.2)	110(74.8)	0.000
Hypoalbuminemia[n(%)]	153(56.7)	54(36.7)	0.000
Diabetes[n(%)]	85(31.5)	48(32.7)	0.806
Hypertension[n(%)]	165(61.1)	111(75.5)	0.003
Heart failure[n(%)]	63(23.3)	45(30.6)	0.105
PAD[n(%)]	22(8.1)	17(11.6)	0.252
Stroke[n(%)]	89(33.0)	46(31.3)	0.728
Malignant tumor[n(%)]	106(39.3)	42(28.6)	0.029
MODS[n(%)]	62(23.0)	38(25.9)	0.509
RRT[n(%)]	50(18.5)	33(22.4)	0.337
Cause of disease[n(%)]			0.083
Infection	103(38.1)	37(25.2)	
Carciac functional insufficiency	28(10.4)	17(11.6)	
Hypovolemia	74(27.4)	44(29.9)	
Drug	23(8.5)	19(12.9)	

AKI: acute kidney injury; AonC: acute on chronic kidney disease; eGFR: estimated glomerular filtration rate; SCr: serum creatinine; BUN: blood urea nitrogen; PAD: peripheral arterial disease; RRT: renal replacement therapy; MODS: mutliple organ dysfunction syndrome

表2 单纯AKI与AonC患者预后比较

Table 2 Comparison of prognosis between denovo AKI and AonC groups [n(%)]

Prognosis	Denovo AKI group(n=270)			AonC group(n=147)		
	Follow-up 30 days	Follow-up 90 days	Follow-up 1 year	Follow-up 30 days	Follow-up 90 days	Follow-up 1 year
Death	137(50.7)	156(57.8)	170(63.0)	58(39.5)*	72(49.0)	84(57.1)
Loss of follow-up	13(4.8)	18(12.2)	22(8.1)	10(6.8)	15(10.2)	18(12.3)
Survival	120(44.4)	96(35.6)	78(28.9)	79(53.7)	60(40.8)	45(30.6)

AKI: acute kidney injury; AonC: acute on chronic kidney disease. Compared with denovo AKI group, * $P<0.05$

表3 Cox多因素分析随访30 d死亡危险因素

Table 3 Multivariate analysis of risk factors for death at 30 days followed-up with Cox proportional hazards model

Risk factor	B	SE	Wald	HR	95% CI	P value
AKI Ⅰ	13.068	0.001				
AKI Ⅱ	0.600	0.186	10.367	1.822	1.265-2.626	0.001
AKI Ⅲ	0.640	0.199	10.387	1.897	1.285-2.800	0.001
Anemia	0.831	0.205	16.390	2.297	1.536-3.435	0.000
Hypoalbuminemia	0.448	0.164	7.457	1.565	1.135-2.158	0.006
Heart failure	0.411	0.168	5.975	1.508	1.085-2.096	0.015
Malignant tumor	0.352	0.155	5.178	1.421	1.050-1.924	0.023
MODS	0.382	0.161	5.620	1.465	1.068-2.008	0.018
RRT	-0.639	0.195	10.718	0.528	0.360-0.774	0.001

AKI: acute kidney injury; MODS: mutliple organ dysfunction syndrome; RRT: renal replacement therapy

表4 不同eGFR水平组AonC患者的病死率比较

Table 4 Comparison of mortality of AonC patients with different eGFR [n(%)]

eGFR[ml/(min·1.73 m^2)]	n	Follow-up 30 days	Follow-up 90 days	Follow-up 1 year
60–45	66	26(39.4)	32(48.5)	37(56.1)
45–30	41	19(46.3)	22(53.7)	24(58.5)
30–15	28	9(32.1)	14(50.0)	17(60.7)
<15	12	4(33.3)	4(33.3)	6(50.0)
P value		0.651	0.670	0.928

eGFR: estimated glomerular filtration rate; AonC: acute on chronic kidney disease

本研究表明单纯AKI患者30 d病死率高于AonC患者,差异具有统计学意义,而90 d及1年病死率无差异,不同eGFR水平的AonC患者30 d、90 d和1年的病死率无差异。Hsu等[13]研究了AonC患者的短期和长期预后,结果显示基础eGFR<15 ml/(min·1.73 m^2)的院内病死率最低,但此研究没有分析各组AKI分期的差异。本研究结果提示,基础eGFR水平越低AKI分期可能会越低,故上述研究中病死率低可能是由于AKI严重程度低所致。另有学者将AKI患者基础肾功能水平与院内死亡风险进行交叉分析,结果表明AKI Ⅰ期、Ⅱ期两组患者中基础eGFR值与死亡风险无相关性;AKI Ⅲ期患者中基础eGFR>60 ml/(min·1.73 m^2)者的死亡风险最高,提示AKI Ⅲ期患者合并慢性肾功能不全可能死亡风险相对较低,但是各个基础eGFR水平分层研究后均显示AKI分期越高,死亡风险也越高[1]。本研究结果与上述文献报告基本一致,由此我们认为,AKI分期及是否合并营养不良和多脏器功能损害是老年AKI患者近期死亡风险的重要影响因素,而非基础肾功能水平。CKD患者在临床上易受关注,肾功能指标能得到密切监测,故此类患者并发多脏器功能不全及死亡风险反而较小;因此对于存在感染、容量不足、心力衰竭和应用抗生素的非CKD老年患者也应高度重视其发生AKI的可能性,注意管理合并症。赵佳慧等[12]发现需要透析的AKI患者中,存在CKD的患者5年病死率明显增高,说明AKI发病前存在基础CKD对长期预后有严重影响。

以往研究证实,AKI增加老年患者进展至终末期肾病(end stage renal disease, ESRD)的风险[14];肾功能未恢复患者5年内死亡或发生ESRD的比例高于肾功能恢复患者[1];即使肾功能完全恢复的患者仍然可能逐渐进展为CKD[1];AonC患者近期预后虽然并不差于单纯AKI患者,但是5~10年病死率和(或)维持血液透析治疗的比例明显增高。因此,虽然本研究存活患者中单纯AKI组和AonC组90 d和1年肾功能恢复率无显著差异,但是老年AKI患者基础肾功能对远期预后的影响还需进行长期的观察、研究和评估。

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