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(收稿日期: 2021-08-23)

(修回日期: 2021-09-14)

急性 A 型主动脉夹层患者术后急性肾损伤 发生的危险因素分析

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摘要 目的 讨论急性 A 型主动脉夹层患者术后发生急性肾损伤 (acute kidney injury, AKI) 的危险因素。**方法** 回顾性分析 2020 年 1~12 月在南京鼓楼医院行急诊手术治疗的 211 例主动脉夹层患者的临床资料。根据术后是否发生 AKI 将患者分为 AKI 组和非 AKI 组。采用单因素及多因素 Logistic 分析建立回归模型, 筛选出与 AKI 相关的独立危险因素。**结果** 术后 105 例患者发生了 AKI, 发生率为 47.8%; 单因素分析结果显示, 术前白细胞、肾小球滤过率、尿素氮及肌酐、肾功能不全病史、手术时

基金项目: 南京大学现代医院管理与发展研究所项目; 南京鼓楼医院医学发展医疗救助基金会资助项目 (NDYG2021052)

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间、术中出血量及尿量、术后 1 天尿素氮、肌酐及胱抑素 C 与术后 AKI 的发生相关($P < 0.05$)。多因素 Logistic 回归分析显示,术后 1 天肌酐(OR = 1.020, 95% CI: 1.007 ~ 1.033, $P = 0.003$)、术后 1 天尿素氮(OR = 1.287, 95% CI: 1.098 ~ 1.507, $P = 0.002$)及术后 1 天胱抑素 C(OR = 3590.873, 95% CI: 96.335 ~ 133849.038, $P < 0.001$)与术后 AKI 发生独立相关;AKI 组患者 ICU 住院天数及总住院天数均大于非 AKI 组($t = 3.225, P = 0.001$; $t = 2.317, P = 0.021$)。结论 术后 1 天尿素氮、肌酐及胱抑素 C 升高是急性 A 型主动脉夹层术后 AKI 的独立危险因素,其中胱抑素 C 能早期灵敏预测术后 AKI 的发生。AKI 的发生会增加患者的 ICU 住院天数及总的住院天数,可能会增加患者的医疗费用。

关键词 Sanford A 型主动脉夹层 急性肾损伤 危险因素

中图分类号 R614

文献标识码 A

DOI 10.11969/j.issn.1673-548X.2022.02.030

Analysis of Risk Factors for Postoperative Acute Kidney Injury in Acute Stanford Type A Aortic Dissection. ZHU Xuewen, LUO Xuan.

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Abstract Objective To analyze the risk factors of AKI in patients with acute type A aortic dissection. **Methods** From January to December 2020, the clinical data of 211 patients with acute type A aortic dissection undergoing emergency operation in Drum Tower hospital were analyzed. All patients were divided into AKI group and non - AKI group according to the occurrence of AKI. Univariate and multivariate Logistic analysis was used to establish the regression model and screen the independent risk factors related to AKI. **Results** One hundred and five patients had AKI, that was the incidence was 47.8%. The results of univariate analysis showed that preoperative leukocyte, renal glomerular filtration rate, urea nitrogen and creatinine, history of renal insufficiency, time of operation, intraoperative bleeding and urinary volume, postoperative urea nitrogen, creatinine and cystatin C were associated with the occurrence of AKI ($P < 0.05$). Multivariate Logistic regression analysis showed that the creatinine [odds ratio (OR) = 1.020, 95% CI: 1.007 ~ 1.033, $P = 0.003$], the urea nitrogen (OR = 1.287, 95% CI: 1.098 ~ 1.507, $P = 0.002$) and the cystatin C (OR = 3590.873, 95% CI: 96.335 ~ 133849.038, $P < 0.001$) were independently associated with the occurrence of AKI. The length of stay in ICU and total length of hospital stay in AKI group were longer than that in non - AKI group ($t = 3.225, P = 0.001$; $t = 2.317, P = 0.021$; respectively). **Conclusion** Elevated urea nitrogen, creatinine and cystatin C of one day after operation are independent risk factors for AKI. The Cystatin C can sensitively predict the early occurrence of AKI. The occurrence of AKI may increase the length of stay in ICU and the total length of hospital stay, and may increase hospital cost.

Key words Stanford type A aortic dissection; Acute kidney injury; Risk factors

急性 A 型主动脉夹层(aortic dissection, AD)是一种最致命的心血管外科疾病,发病后其病死率以每小时 1% ~ 2% 递增,病情发展急骤,如不及时治疗病死率极高^[1,2]。目前治疗 AD 以外科手术为首选,患者术前由于全身血管病变累及不同脏器造成灌注不良、术中手术操作复杂、手术时间长等原因,术后容易出现各类并发症,其中急性肾损伤(acute kidney injury, AKI)尤为常见,既往研究报道 AD 术后 AKI 发生率为 44% ~ 54%^[3~5]。AKI 的发生不仅增加了患者术后住院时间和费用,而且严重的 AKI 会造成患者严重的不良后果,甚至死亡^[6,7]。因此早期识别 AD 患者术后 AKI 发生相关的危险因素,从而指导临床采取有针对性的预防措施,并进一步改善患者的预后具有重要意义。本研究通过回顾性分析行急诊手术治疗的 AD 患者的临床资料,探讨与 AKI 发生相关的独立危险因素,为临床预防和治疗 AKI 提供相应的依据。

资料与方法

1. 一般资料:回顾性分析于 2020 年 1 ~ 12 月在南京大学附属南京鼓楼医院行急诊手术治疗的 226

例 AD 患者的临床资料。纳入标准:所有患者术前均经过严格的病史采集、心脏超声和主动脉 CTA 等检查确诊为 Stanford A 型主动脉夹层,发病时间均在 48h 以内。排除标准:未行手术患者,术中因无法停机死亡患者,术后 48h 内死亡患者。最终入选 211 例患者,其中男性 166 例,女性 45 例,平均年龄 54.6 ± 12.9 岁。本研究通过笔者医院医学伦理学委员会审批。

2. 研究方法:记录患者入院时年龄、性别、体重指数、高血压、糖尿病、冠心病及肾功能不全病史及术前白细胞、血小板、肌酐及尿素氮、BNP 等数值。查阅 CTA 记录左右肾动脉供血情况,分为真腔供血、假腔供血、真 - 假腔供血。收集手术时间、体外循环时间、深低温停循环时间、阻断时间、术中出血量、输血量、尿量、术后 1 天尿素氮、肌酐、胱抑素 C 等,记录 ICU 停留时间及住院天数。术后 AKI 诊断采用 2005 年急性肾损伤网络工作小组制定的 AKIN 诊断标准,根据患者术后是否发生 AKI 分为 AKI 组和非 AKI 组。

3. 手术方式:手术均采用全身麻醉下深低温(鼻咽温 20 ~ 22℃),下半身停循环并行低流量选择性脑

灌注。术中根据夹层破口位置选择不同手术方式,主要包括 Bentall、David、Wheats + 升主动脉置换 + 全弓置换,升主动脉置换 + 全弓置换(岛状吻合),升主动脉置换 + 全弓覆膜支架置入,升主动脉置换 + 右半弓置换术,同期行冠状动脉旁路移植术及二尖瓣成形/置换术,详见表 1。

表 1 按照主动脉弓部手术处理分类的手术方式

同期手术	全弓置换	全弓置换 (岛状吻合)	全弓覆膜 支架置入	右半弓	合计
n	50	33	90	38	211
Bentall 手术	9	4	12	18	43
David 手术	1	0	0	0	1
Wheats 手术	0	0	0	1	1
升主动脉置换	35	26	75	17	153
二尖瓣成形/置换	2	2	1	1	6
CABG 手术	3	1	2	1	7

4. 统计学方法:应用 SPSS 19.0 统计学软件对数据进行统计分析,连续变量用均数 \pm 标准差 ($\bar{x} \pm s$) 表示,采用 t 检验(正态分布);分类变量资料用频率 (%) 表示,组间率的比较采用 χ^2 检验,以 $P < 0.05$ 为差异有统计学意义。将组间差异有统计学意义的指标纳入多因素 Logistic 回归分析,筛选出术后早期 AKI 发生的危险因素。

结 果

1. 临床资料比较:术后 105 例患者发生了 AKI,发生率为 47.8%,其中 22 例患者术后需行 CRRT 治疗,有 10 例患者 30 天内死亡,其 30 天内病死率 9.5%。两组患者一般资料、术中及术后相关资料比较,术前白细胞、肾小球滤过率、尿素氮及肌酐、肾功能不全病史、手术时间、术中出血量及尿量、术后 1 天尿素氮、肌酐及胱抑素 C 比较,差异有统计学意义 ($P < 0.05$),详见表 2。

表 2 两组患者相关临床资料的比较 [$n(\%)$, $\bar{x} \pm s$]

项目	AKI 组	非 AKI 组	P
男性	88(83.8)	78(73.6)	0.092
年龄(岁)	54.1 ± 13.1	55.1 ± 12.8	0.606
BMI(kg/m^2)	23.9 ± 1.5	23.8 ± 1.6	0.880
冠心病	5(4.7)	8(7.5)	0.569
肾功能不全	5(4.7)	0(0)	0.029
心包积液	52(49.5)	53(50.0)	0.582
二次转机	1(0.9)	2(1.8)	0.999
手术时间(min)	423.9 ± 104.4	389.3 ± 89.5	0.011
转机时间(min)	219.2 ± 69.6	202.8 ± 61.1	0.071
阻断时间(min)	159.1 ± 50.4	147.8 ± 47.3	0.096
深停时间(min)	29.3 ± 11.2	29.7 ± 11.1	0.795
出血量(ml)	2130.2 ± 1029.5	1788.6 ± 798.9	0.008
输血量(ml)	2402.7 ± 1033.9	2210.1 ± 854.5	0.142
尿量(ml)	1206.2 ± 1178.3	1498.9 ± 914.4	0.045
术前白细胞计数($\times 10^9/\text{L}$)	12.2 ± 4.1	10.8 ± 3.9	0.006
术前血红蛋白(g/dl)	119.7 ± 26.2	121.6 ± 23.5	0.588
术前血小板计数($\times 10^9/\text{L}$)	149.1 ± 69.2	153.1 ± 71.3	0.681
活化部分凝血活酶时间(s)	30.6 ± 7.7	29.7 ± 7.8	0.432
血浆纤维蛋白原(g/L)	2.5 ± 1.4	2.7 ± 1.5	0.297
术前肾小球滤过率(ml/min)	53.4 ± 31.9	96.4 ± 29.8	<0.001
术前尿素氮(mmol/L)	9.9 ± 5.7	6.9 ± 2.2	<0.001
术前肌酐($\mu\text{mol}/\text{L}$)	159.6 ± 182.2	74.1 ± 24.4	<0.001
术后 1 天尿素氮(mmol/L)	14.4 ± 4.4	8.3 ± 3.9	<0.001
术后 1 天肌酐($\mu\text{mol}/\text{L}$)	193.1 ± 102.3	80.1 ± 35.3	<0.001
术后 1 天胱抑素 C(mg/L)	1.6 ± 0.6	0.8 ± 0.1	<0.001
术前 D-二聚体(mg/L)	17.6 ± 38.2	20.1 ± 62.1	0.736
术前 B 型利钠肽(pg/ml)	182.5 ± 403.1	104.3 ± 150.7	0.063
左肾动脉真腔供血	60(57.1)	70(66.0)	0.204
左肾动脉假腔供血	26(24.7)	18(16.9)	0.179
左肾动脉真-假腔供血	18(17.1)	19(17.9)	0.999
右肾动脉真腔供血	71(67.6)	84(79.2)	0.063
右肾动脉假腔供血	19(18.1)	10(9.4)	0.075
右肾动脉真-假腔供血	16(15.2)	13(12.2)	0.555
ICU 天数(天)	9.5 ± 11.3	5.6 ± 4.8	0.001
住院天数(天)	21.1 ± 12.2	17.8 ± 6.9	0.021

2. 危险因素回归分析: 将单因素分析中有统计学意义的指标引入多因素 Logistic 回归分析中显示, 术后 1 天肌酐(OR = 1.020, 95% CI: 1.007 ~ 1.033, P = 0.003)、术后 1 天尿素氮(OR = 1.287, 95% CI: 1.098 ~ 1.507, P = 0.002) 及术后 1 天胱抑素 C (OR = 3590.873, 95% CI: 96.335 ~ 133849.038, P < 0.001) 与术后 AKI 发生独立相关, 详见表 3。

表 3 术后发生 AKI 的独立危险因素的 Logistic 分析

因素	OR	95% CI	P
手术时间	0.999	0.993 ~ 1.005	0.753
术中出血量	1.001	1.000 ~ 1.001	0.082
术中尿量	1.000	0.999 ~ 1.000	0.476
术前肾小球滤过率	1.003	0.977 ~ 1.030	0.800
术前白细胞	1.160	0.999 ~ 1.347	0.052
术前肌酐	0.995	0.978 ~ 1.013	0.602
术前尿素氮	0.981	0.978 ~ 1.013	0.887
术后 1 天肌酐	1.020	1.007 ~ 1.033	0.003
术后 1 天尿素氮	1.287	1.098 ~ 1.507	0.002
术后 1 天胱抑素 C	3590.873	96.335 ~ 133849.038	< 0.001

讨 论

AD 患者由于夹层病变累及全身多处血管会导致重要脏器的灌注不良, 加之手术操作复杂、时间长、出血多、需要停循环操作等, 所以患者术后并发症多, 其中 AKI 是最常见并发症之一^[1,8]。文献报道 AD 患者的术后 AKI 的发生率为 44% ~ 54%, 本研究结果发现术后 AKI 的发生率为 47.8%, 与既往文献报道相一致。导致 AD 患者术后 AKI 发生的影响因素很多, 年龄、术前肌酐异常、长时间呼吸机使用、输血、BMI、C 反应蛋白、术前肾功能不全及肾阻力指数等是术后 AKI 发生的独立危险因素^[6,9~16]。本研究结果显示, 术后 1 天尿素氮、肌酐及胱抑素 C 升高是 AD 术后 AKI 的独立危险因素, 两组患者术前尿素氮及肌酐水平具有明显差异, 提示患者术前已经存在肾功能损伤, 造成纳入多因素研究后并没成为术后 AKI 发生的独立危险因素, 考虑部分患者手术治疗改善了肾脏的灌注, 从而没有进一步发展为 AKI, 而术后 1 天的尿素氮及肌酐水平能够反映患者术后的即时肾功能, 所以一旦术后尿素氮及肌酐明显持续升高需要临床医生高度重视, 提前做好干预措施。术后 AKI 的诊断是依据血肌酐水平、肾功能和尿量, 肌酐被认为是相对特异性的指标, 但并不特别敏感, 因为在肾功能小于正常值 50% 之前, 肌酐水平不会显著增加。此外, 肌酐水平受多种因素影响, 包括肌肉质量、饮

食、肾小管分泌异常以及各种药物和内源性物质^[17]。最近胱抑素 C 用于 AKI 的早期诊断, 据报道血清胱抑素 C 预测 AKI 比肌酐提前 1 ~ 2 天^[18]。胱抑素 C 不易受到其他常规测量肾功能方法的干扰, 能够准确并有效预测 AKI^[19,20]。本研究结果也表明, 术后 1 天胱抑素 C 水平是 AD 术后发生 AKI 的独立危险因素。

大量研究证明, AD 患者术后发生 AKI 后会增加住院天数和费用, 并增加了术后 30 天内的病死率^[7,15,21]。本研究发现, AKI 组患者 ICU 住院天数及总的住院天数均远高于非 AKI 组, 其中 AKI 组患者中有 22 例需行 CRRT 支持治疗, CRRT 使用率为 20.9%, 30 天内的病死率为 9.5%, CRRT 的使用率稍高于文献报道但病死率低于文献报道^[3,15,22]。考虑一方面与本研究收治的患者病情较重, 所有患者均是 24h 内急诊手术完成, 手术时间长且复杂, 术后肾功能损伤重, 需要 CRRT 辅助治疗; 另一方面与术后对 AKI 治疗干预比较积极有关, 中心拥有丰富经验治疗 AKI。术后 AKI 的预防治疗需要临床医生早期准确识别其发生的高危因素, 筛选出高危 AKI 患者, 通过本中心的研究能够为 AD 患者术后 AKI 的发生预测提供临床思路。

本研究注重预测 AD 患者急诊术后早期的 AKI 发生, 纳入的研究因素都是术前、术中及术后早期的临床数据, 其结果更具有 AKI 发生的早期预测价值。研究结果再次证明胱抑素 C 的升高能够预测 AKI 的发生, 而且统计学结果发现胱抑素 C 与 AKI 的发生关联性更强, 其敏感度高, 能够早期预测术后 AKI 的发生。

本研究也存在一定的局限性: ①本研究为单中心回顾性研究, 仅代表笔者医院 AD 患者的 AKI 发生情况; ②本研究仅收集了 1 年的患者病例数, 样本量不够大, 可能影响对术后 AKI 高危因素的精准分析, 需要进一步进行更大样本量、设计更科学的研究。

综上所述, AKI 是 AD 患者术后常见的并发症, 术后 AKI 的发生是患者早期不良预后的危险因素。术后 1 天尿素氮、肌酐及胱抑素 C 升高是 AD 术后 AKI 的独立危险因素, 其中胱抑素 C 能早期灵敏预测术后 AKI 的发生。本研究对于 AD 患者术后可能出现 AKI 高危患者的早期识别、早期预防、早期治疗具有重要的临床意义。

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(收稿日期: 2021-08-22)

(修回日期: 2021-09-15)

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(收稿日期: 2021-08-03)

(修回日期: 2021-09-23)