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血清乳酸脱氢酶水平与住院患者急性肾损伤的相关性研究及预后风险评估

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摘　要

目的：探讨血清乳酸脱氢酶(LDH)水平与住院患者急性肾损伤(AKI)及死亡风险的相关性，为早期识别AKI提供指导。方法：纳入2023年1月至2023年12月在本院的4909例患者，对患者临床数据进行回顾性收集。根据血清LDH水平的四分位数将患者分为四组(Q1~Q4组)，比较各组患者基线特征，使用logistic回归模型评估不同LDH组与住院患者AKI的相关性，探究LDH水平对AKI患者死亡的影响。进行亚组分析，以确定LDH水平与住院患者发生AKI风险在不同亚组间是否有差异。使用受试者工作特征(ROC)曲线评估LDH的预测效能。结果：4909例患者中有850例发生AKI，占总人群17.32%。AKI发生率随着LDH水平的增加而增加(12.96% vs. 13.45% vs. 18.09% vs. 22.78%)。在未校正的logistic回归分析中，与对照组Q1相比，Q3组(OR 1.49, 95% CI 1.19~1.85, $P < 0.01$)和Q4组(OR 2.21, 95% CI 1.79~2.74, $P < 0.01$)发生AKI的风险更高。使用模型1校正混杂因素后，Q3组和Q4组的调整OR (95% CI)分别为1.49 (1.20~1.87)和2.20 (1.78~2.72)。经模型2调整后观察到类似结果，Q3组、Q4组的OR分别为1.44、1.89，95% CI分别为1.19~1.85、1.51~2.38，Q3组$P = 0.002$，Q4组<0.001。在未调整的logistic回归分析中，与Q1组相比，Q4组(OR 5.07, 95% CI 1.97~13.09, $P = 0.001$)的AKI患者发生死亡的风险较高。使用模型1校正混杂因素后，Q4组的调整OR (95% CI)为5.30 (2.04~13.77)。经模型2校正后观察到类似结果，Q2组、Q4组的OR分别为3.90、2.97，95% CI分别为1.24~12.24、1.05~8.46。ROC曲线显示LDH对住院患者发生AKI具有预测价值，曲线下面积(AUC)为0.59 (95% CI 0.56~0.62, $P < 0.05$)。LDH预测AKI患者死亡的AUC为0.70 (95% CI 0.67~0.73, $P < 0.05$)，当血清LDH水平与血清肌酐(Scr)结合起来预测住院患者AKI风险及AKI患者的住院死亡时，ROC曲线面积分别提高至0.60和0.80。结论：高水平血清LDH与住院期间发生AKI的风险独立相关，且LDH水平越高，AKI患者的死亡率越高。监测住院患者血清LDH水平可为早期识别AKI、改善患者预后提供指导。

关键词

急性肾损伤，乳酸脱氢酶，危险因素，死亡率

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A Study on the Correlation between Serum Lactate Dehydrogenase Level and Acute Kidney Injury in Hospitalised Patients and Prognostic Risk Assessment

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Abstract

Objective: To explore the relationship between serum lactate dehydrogenase (LDH) levels and acute kidney injury (AKI) in hospitalized patients to guide the early identification of AKI. Methods: This study included 4909 patients hospitalized in our hospital from January 2023 to December 2023, and patients' clinical data were retrospectively collected. The study population was divided into four groups (groups Q1~Q4) according to the quartile of serum LDH levels. Differences in baseline characteristics between the 4 groups were compared. Using logistic regression models to evaluate the association of different serum LDH groups with AKI in hospitalized patients and investigating the effect of LDH levels on mortality in patients with AKI. Subgroup analyses were performed to examine differences in the association between LDH levels and the risk of developing AKI in hospitalized patients in different subgroups. ROC curve was used to assess the predictive performance of LDH. Results: AKI occurred in 850 of 4909 patients, representing 17.32% of the total population. AKI incidence increases with increasing LDH levels (12.96% vs. 13.45% vs. 18.09% vs. 22.78%). In unadjusted logistic regression analysis, the risk of AKI was higher in the Q3 (OR 1.49, 95% CI 1.19~1.85, $P < 0.01$) and Q4 (OR 2.21, 95% CI 1.79~2.74, $P < 0.01$) groups compared with the control group Q1. After adjustment for confounders using model 1, the adjusted OR (95% CI) was 1.49 (1.20~1.87) and 2.20 (1.78~2.72) for the Q3 and Q4 groups, respectively. Similar results were observed after adjustment using model 2, the ORs of the Q3 and Q4 groups were 1.44 and 1.89, respectively, with 95% CIs of 1.19~1.85 and 1.51~2.38, respectively, and P values of 0.002 and <0.001, respectively). In unadjusted logistic regression analysis, the risk of mortality in AKI patients was higher in the Q4 (OR 5.07, 95% CI 1.97~13.09, $P = 0.001$) compared with the control group Q1. After adjusting for the confounders using model 1, the adjusted OR (95% CI) was 5.30 (2.04~13.77) for the Q4 group. Similar results were observed after adjustment by model 2, the ORs of the Q2 and Q4 groups were 3.90 and 2.97, respectively, with 95% CIs of 1.24~12.24 and 1.05~8.46, $P < 0.05$. The ROC curve showed the predictive value of LDH for the development of AKI in hospitalized patients, with an area under the curve of 0.59 (95% CI 0.56~0.62, $P < 0.05$). The AUC for LDH in predicting death among patients with AKI was 0.70 (95% CI 0.67~0.73, $P < 0.05$). When serum LDH levels are combined with serum creatinine (Scr) to predict the risk of AKI in hospitalized patients and the in-hospital mortality of AKI patients, the ROC curve areas increase to 0.60 and 0.80, respectively. Conclusion: High serum LDH levels were independently associated with the risk of AKI during hospitalization, and higher LDH levels were associated with higher mortality in patients with AKI. Monitoring the serum LDH level in hospitalized patients can provide guidance for early detection of AKI.

Keywords

Acute Kidney Injury, Lactate Dehydrogenase, Risk Factors, Mortality

1. 引言

急性肾损伤(Acute kidney injury, AKI)被定义为各种诱因引起的肾功能突然下降，导致肾小球滤过率下降、尿素和含氮废物潴留、水和电解质失衡，与住院时间延长、慢性肾脏病及死亡率增加相关[1] [2]。据统计，AKI 在成人住院患者中的发生率约 20%，重症监护病房的患者中发病率上升近 60% [3]。此外，肾功能持续丧失可能会增加患慢性肾脏病(chronic kidney disease, CKD)和终末期肾病的风险[4]。AKI 会导致不同程度的不可逆肾单位损失、间质纤维化，并可能进展为 CKD。目前 AKI 治疗的核心是针对 AKI 的病因进行治疗，并侧重于保护组织灌注、加强治疗监测，对症治疗及预防并发症。从治疗的角度来看，减少肾小管坏死和保护剩余肾单位的药物是降低 AKI 急性期死亡率和延缓慢性进展的最佳选择。然而，目前尚未开发出能够兼顾阻断肾小管细胞坏死而不引起因大量细胞的脱氧核糖核酸损伤而导致的恶性肿瘤[5]。由于 AKI 目前尚无特异性治疗方法，早期识别 AKI 患者，及时进行干预从而改善预后尤为重要。乳酸脱氢酶(Lactate dehydrogenase, LDH)是自然界最常见的酶之一，主要由两个亚基 LDHA 和 LDHB 组成的四聚体酶[6]。LDH 在体内的作用是将乳酸和氧化型烟酰胺腺嘌呤二核苷酸(Nicotinamide adenine dinucleotide, NAD)分别转化为丙酮酸和还原型烟酰胺腺嘌呤二核苷酸(Nicotinamide adenine dinucleotide Hydride, NADH)，广泛存在于机体各种组织中，以心肌、骨骼肌和肾脏中含量最为丰富[7]。细胞损伤坏死后，LDH 被释放到血清中，导致 LDH 水平升高[8]。有研究表明，血清 LDH 在心肌梗死[9]、肺损伤[10]、脓毒血症[11]、恶性肿瘤[12]等患者中呈高水平。此外，LDH 与疾病严重程度有关，较高的 LDH 水平与重症患者的较高死亡率有关，包括患有新冠肺炎病和其他疾病的患者[13] [14] [15]。有研究发现，LDH 水平与 AKI 危重患者的死亡率独立相关[16]。然而，LDH 水平与住院患者发生 AKI 的关系尚不清楚。因此，本研究旨在探究血清 LDH 水平对住院患者发生 AKI 的预测价值及对 AKI 患者死亡的影响。

2. 对象与方法

2.1. 研究对象

回顾性收集 2023 年 1 月至 2023 年 12 月于本单位住院的 6040 例患者的资料，根据纳入排除标准最终 4909 例患者纳入研究。排除标准：(1) 年龄 < 18 岁；(2) 住院时间 < 48 小时；(3) 合并尿毒症、进行肾脏替代治疗或行肾移植术；(4) 相关数据缺失。本研究经本单位医学伦理委员会批准。

2.2. AKI 定义

AKI 的诊断和分期标准采用 2012 年改善全球肾脏病预后组织(Kidney Disease: Improving Global Outcomes, KDIGO)指南，符合以下任何一项者可诊断为 AKI。(1) 48 小时内血清肌酐(Serum creatinine, Scr)值较基线上升超过 26.5 μmol/L (0.3 mg/dL)；(2) 7 天内 Scr 较基线上升超过 1.5 倍。基线 Scr 值为住院期间第一次检测的 Scr 值。

2.3. 资料收集

收集包括年龄、性别、体重指数、手术史、吸烟史、饮酒史、住院天数、实验室检查指标、合并症、药物使用等人口学和临床资料。其中患者的合并症据国际疾病分类第十一次修订中的标准进行诊断。使用 CKD-EPI 公式计算估算肾小球滤过率(estimated glomerular filtration rate, eGFR)。

2.4. 统计学方法

采用 SPSS 25.0、R 软件进行统计分析，缺失值超过 15%的变量被排除，缺失值及剔除的异常数据使用多重插补法进行插补。根据血清 LDH 水平的四分位数将研究对象分为四组(Q1~Q4 组)。连续变量以$\bar{x} \pm s$表示，组间比较采用方差分析或 Kruskal-Wallis 检验。分类变量以频数表示(百分比)表示，组间比较采用卡方检验或 Fisher 精确检验。为了验证 LDH 水平与住院患者发生 AKI 及 AKI 患者死亡的相关性，采用逐步回归分析为logistic回归模型筛选协变量，并采用4节点限制性立方样条图(Restricted cubic spline, RCS)模型，探讨 LDH 与 AKI 风险之间的非线性相关性。绘制受试者工作特征(Receiver operating characteristic, ROC)曲线，计算曲线下面积(Area under curve, AUC)，以评估 LDH 的预测价值。$P < 0.05$ 为差异有统计学意义。

3. 结果

3.1. 研究人群基线特征

最终 4909 例住院患者纳入研究，按照血清 LDH 水平将其分为四组进行基线特征比较(表 1)。住院患者中 850 例发生 AKI，AKI 发生率为 17.32%，死亡率 2.55%。其中，四组患者发生 AKI 的人数分别为 159 例(12.96%)、165 例(13.45%)、222 例(18.09%)和 304 例(22.78%)，AKI 发生率随着 LDH 水平升高而增加($P < 0.01$)。与 LDH 低水平组相比，血清 LDH 高水平组男性、手术史、吸烟者及饮酒者比例较低(均 $P < 0.01$)；血红细胞计数、血小板、白蛋白水平和 eGFR 较低(均 $P < 0.01$)；白细胞计数、转氨酶、总胆红素、尿酸较高(均 $P < 0.01$)；合并症与用药方面，高水平 LDH 组 CKD、高血压比例较高(均 $P < 0.05$)，钙通道阻滞剂、抗生素使用比例较高(均 $P < 0.05$)，住院天数较长($P < 0.01$)，死亡率较高($P < 0.01$)。

Table 1. Comparison of baseline characteristics of patients with different LDH levels
表 1. 不同 LDH 水平患者的基线特征比较

变量	乳酸脱氢酶，U/L				
	Q1 组 ≤149 (n = 1228)	Q2 组 149~177.5 (n = 1227)	Q3 组 177.5~222.5 (n = 1227)	Q4 组 <222.5 (n = 1227)	*P*
年龄，岁	60.24 ± 14.40	62.07 ± 13.21	62.79 ± 13.82	60.38 ± 15.11	<0.001
男性(N, %)	780 (63.52%)	715 (58.27%)	689 (56.15%)	688 (56.07%)	<0.001
体重指数，kg/m^2	23.84 ± 3.58	24.38 ± 3.65	24.54 ± 3.78	24.33 ± 3.94	<0.001
收缩压，mmHg	129.69 ± 18.81	131.72 ± 18.62	134.67 ± 21.02	131.58 ± 21.68	<0.001
舒张压，mmHg	76.55 ± 12.01	77.04 ± 11.56	77.73 ± 12.05	77.19 ± 13.67	0.126
手术史(N, %)	610 (49.67%)	552 (44.99%)	498 (40.59%)	513 (41.81%)	<0.001
吸烟史(N, %)	460 (37.46%)	455 (37.08%)	424 (34.56%)	383 (31.21%)	0.004
饮酒史(N, %)	399 (32.49%)	348 (28.36%)	329 (26.81%)	328 (26.73%)	0.004
红细胞计数，×10^{12}/L	4.15 ± 0.74	4.24 ± 0.73	4.24 ± 0.71	3.98 ± 0.81	<0.001

续表

白细胞计数，$\times10^9$/L	6.38 ± 2.66	6.49 ± 2.63	6.91 ± 2.92	7.99 ± 3.59	<0.001
血红蛋白，g/L	120.94 ± 25.25	126.49 ± 23.46	126.56 ± 23.07	119.12 ± 25.35	<0.001
血小板，$\times10^9$/L	233.82 ± 92.74	223.86 ± 84.66	220.67 ± 87.62	202.72 ± 95.66	<0.001
凝血酶原时间，s	11.03 ± 1.64	10.84 ± 1.56	11.19 ± 1.79	11.95 ± 2.05	<0.001
纤维蛋白原，g/L	3.42 ± 1.14	3.38 ± 1.05	3.47 ± 1.10	3.65 ± 1.32	<0.001
凝血酶时间，s	15.73 ± 2.22	15.62 ± 2.24	15.86 ± 2.44	16.16 ± 2.68	<0.001
白蛋白，g/L	36.82 ± 6.13	38.12 ± 5.89	37.38 ± 6.57	34.68 ± 7.29	<0.001
谷丙转氨酶，U/L	19.34 ± 14.87	19.66 ± 12.70	21.84 ± 14.71	26.87 ± 17.40	<0.001
谷草转氨酶，U/L	17.82 ± 9.75	19.25 ± 8.61	22.02 ± 10.94	28.70 ± 13.94	<0.001
总胆红素，μmol/L	13.63 ± 6.91	14.57 ± 6.71	15.54 ± 7.61	16.91 ± 9.09	<0.001
葡萄糖，mmol/L	5.39 ± 1.47	5.46 ± 1.60	5.67 ± 1.68	5.86 ± 1.86	<0.001
总胆固醇，mmol/L	4.56 ± 1.30	4.77 ± 1.29	4.79 ± 1.38	4.69 ± 1.55	<0.001
甘油三酯，mmol/L	1.23 ± 0.65	1.29 ± 0.66	1.30 ± 0.68	1.36 ± 0.75	<0.001
尿酸，μmol/L	273.98 ± 92.88	280.59 ± 95.99	285.42 ± 105.05	291.50 ± 132.05	0.001
血肌酐，μmol/L	69.89 ± 24.23	69.54 ± 24.64	70.79 ± 26.43	73.71 ± 29.87	<0.001
eGFR, ml/min/1.73m^2	92.05 ± 24.57	90.52 ± 23.41	88.41 ± 26.02	86.19 ± 31.57	<0.001
CKD (N, %)	25 (2.04%)	30 (2.44%)	47 (3.83%)	103 (8.39%)	<0.001
脑梗死(N, %)	62 (5.05%)	64 (5.22%)	71 (5.79%)	78 (6.36%)	0.483
糖尿病(N, %)	208 (16.94%)	200 (16.30%)	187 (15.24%)	190 (15.48%)	0.647
冠心病(N, %)	180 (14.66%)	204 (16.63%)	225 (18.34%)	202 (16.46%)	0.110
高血压(N, %)	329 (26.79%)	380 (30.97%)	407 (33.17%)	368 (29.99%)	0.007
质子泵抑制剂(N, %)	1059 (86.24%)	1070 (87.20%)	1043 (85.00%)	1060 (86.39%)	0.465
ACEI/ARB (N, %)	667 (54.32%)	695 (56.64%)	706 (57.54%)	639 (52.08%)	0.030
利尿剂(N, %)	1013 (82.49%)	1011 (82.40%)	1014 (82.64%)	1009 (82.23%)	0.995
β受体阻滞剂(N, %)	556 (45.28%)	530 (43.19%)	529 (43.11%)	497 (40.51%)	0.125
钙通道阻滞剂(N, %)	255 (20.77%)	314 (25.59%)	392 (31.95%)	415 (33.82%)	<0.001
抗生素(N, %)	897 (73.05%)	867 (70.66%)	882 (71.88%)	932 (75.96%)	0.023
非甾体类抗炎药(N, %)	474 (38.60%)	473 (38.55%)	388 (31.62%)	236 (19.23%)	<0.001
AKI (0 期)	1069 (87.05%)	1062 (86.55%)	1005 (81.91%)	923 (75.22%)	<0.001
AKI (1 期)	136 (11.07%)	139 (11.33%)	180 (14.67%)	225 (18.34%)	
AKI (2 期)	16 (1.30%)	16 (1.30%)	32 (2.61%)	53 (4.32%)	
AKI (3 期)	7 (0.57%)	10 (0.81%)	10 (0.81%)	26 (2.12%)	
住院时间，天	17.21 ± 7.61	17.39 ± 7.87	17.83 ± 8.08	19.11 ± 9.25	<0.001
死亡(N, %)	12 (0.98%)	17 (1.39%)	27 (2.20%)	69 (5.62%)	<0.001

eGFR：估算的肾小球滤过率；CKD：慢性肾脏病；ACEI/ARB：血管紧张素转化酶抑制剂/血管紧张素II受体拮抗剂；AKI：急性肾损伤。

3.2. 血清 LDH 水平与 AKI 发生风险的相关性分析

为了探究 LDH 水平对住院患者发生 AKI 的影响，采用单因素、多因素 logistic 回归进行分析(表 2)。在单因素 logistic 回归分析中，与对照组 Q1 相比，高水平 LDH 组(Q3 组和 Q4 组)患者发生 AKI 的风险更高(均 $P < 0.01$)。模型 1 经年龄、性别、体重指数校正后，与对照组相比，高水平 LDH 组与 AKI 风险显著相关(均 $P < 0.01$)。模型 2 经年龄、性别、体重指数、红细胞计数、血红蛋白、凝血酶时间、白蛋白、谷草转氨酶、总胆红素、胆固醇、吸烟史、糖尿病、冠心病和高血压校正后，高水平 LDH 组患者发生 AKI 的风险分别增加 1.44 与 1.89 倍(均 $P < 0.05$)。

Table 2. Relationship between serum LDH levels and development of AKI in hospitalized patients
表 2. 住院患者血清 LDH 水平与发生 AKI 的关系

模型	OR	95% CI	*P*
未校正			
Q1	参考		
Q2	1.05	0.83~1.32	0.715
Q3	1.49	1.19~1.85	<0.001
Q4	2.21	1.79~2.74	<0.001
模型 1			
Q1	参考		
Q2	1.05	0.83~1.33	0.690
Q3	1.49	1.20~1.87	<0.001
Q4	2.20	1.78~2.72	<0.001
模型 2			
Q1	参考		
Q2	1.08	0.85~1.37	0.534
Q3	1.44	1.15~1.81	0.002
Q4	1.89	1.51~2.38	<0.001

模型 1：经年龄、性别、体重指数校正。模型 2：经年龄、性别、体重指数、红细胞计数、血红蛋白、凝血酶时间、白蛋白、谷草转氨酶、总胆红素、胆固醇、吸烟史、糖尿病、冠心病和高血压校正。

3.3. 血清 LDH 水平与 AKI 患者死亡风险的相关性分析

采用单因素、多因素 logistic 回归分析 AKI 患者血清 LDH 水平与死亡风险的相关性(表 3)。在单因素 logistic 回归分析中，在 AKI 患者中，与对照组相比，Q4 组的 AKI 患者发生死亡的风险增高($P = 0.01$)。模型 1 经年龄、性别、体重指数校正后，Q4 组 AKI 患者死亡风险增加 5.30 倍($P < 0.01$)。模型 2 经年龄、性别、体重指数、收缩压、白细胞计数、血红蛋白、胆固醇、谷草转氨酶、CKD、冠心病、ACEI/ARB、抗生素和非甾体类抗炎药校正后，Q2 及 Q4 组 AKI 患者死亡风险分别增加 3.90 和 2.97 倍(均 $P < 0.05$)。

3.4. 血清 LDH 水平对 AKI 住院患者全因死亡的影响

本研究进一步探究了 LDH 水平与 AKI 风险及 AKI 患者死亡之间是否存在非线性相关性。基于 logistic 回归分析的 RCS 模型显示，LDH 水平与 AKI 风险呈线性，AKI 的风险随着 LDH 水平升高而增加，当

LDH > 178 U/L 时，对应的 OR 值 > 1 (图 1)。

Table 3. Relationship between serum LDH levels and in-hospital mortality in patients with AKI
表 3. AKI 患者血清 LDH 水平与住院死亡的关系

模型	OR	95% CI	*P*
未校正			
Q1	参考		
Q2	2.63	0.92~7.57	0.072
Q3	2.23	0.79~6.27	0.128
Q4	5.07	1.97~13.09	0.001
模型 1			
Q1	参考		
Q2149~177.5	2.66	0.92~7.70	0.071
Q3177.5~222.5	2.08	0.73~5.89	0.168
Q4 > 222.5	5.30	2.04~13.77	0.001
模型 2			
≤149	参考		
149~177.5	3.90	1.24~12.24	0.020
177.5~222.5	1.98	0.64~6.06	0.234
>222.5	2.97	1.05~8.46	0.041

模型 1：经年龄、性别、体重指数校正。模型 2：经年龄、性别、体重指数、收缩压、白细胞计数、血红蛋白、胆固醇、谷草转氨酶、CKD、冠心病、ACEI/ARB、抗生素和非甾体类抗炎药校正。

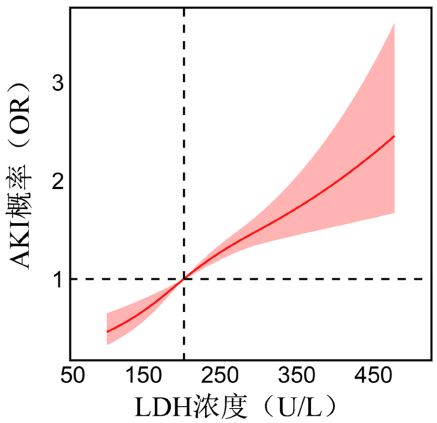

Figure 1. Correlation of serum LDH levels with AKI risk in hospitalized patients assessed using RCS
图 1. 使用 RCS 评估血清 LDH 水平与住院患者 AKI 风险的相关性

最后，使用 ROC 曲线分析来阐明 LDH 的预测效能。单一预测指标 LDH 对住院患者 AKI 风险预测的 AUC 为 0.59 (95% CI 0.56~0.62, $P < 0.05$)，而当血清 LDH 与 Scr 结合起来预测住院患者 AKI 风险时，结果显示 AUC 提高至 0.60 (95% CI 0.57~0.63, $P < 0.05$) (图 2(a)、图 2(b))。此外，LDH 预测 AKI 患者死亡风险的 AUC 为 0.70 (95% CI 0.67~0.73, $P < 0.05$)，当血清 LDH 水平与 Scr 结合起来预测 AKI 患者的住院死亡时，AUC 提高至 0.80 (95% CI 0.77~0.83, $P < 0.05$) (图 2(c)、图 2(d))。

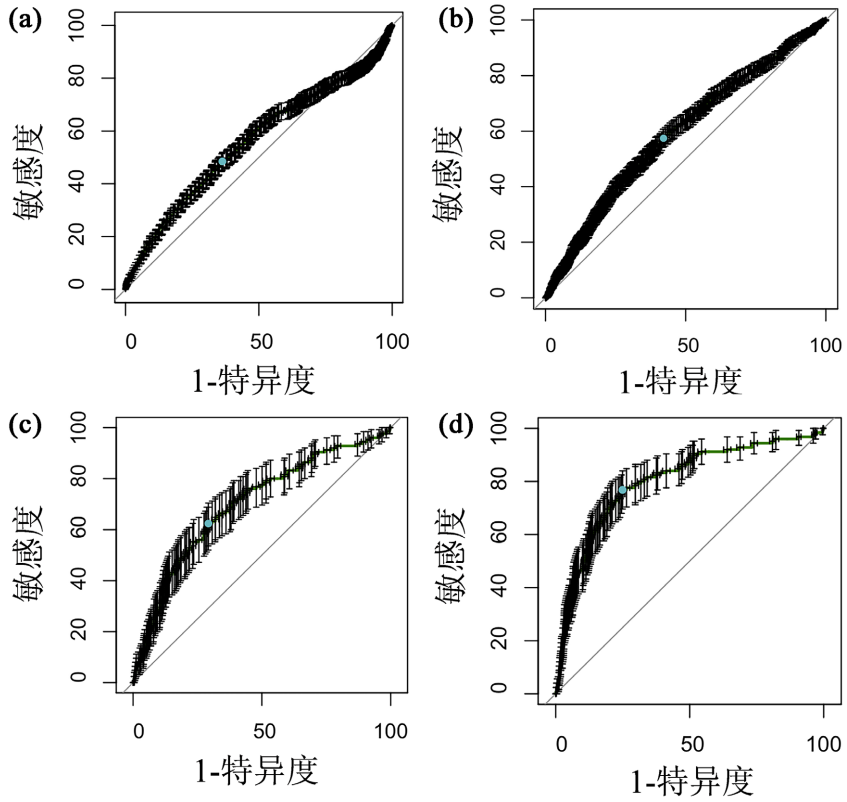

Figure 2. ROC curves of LDH alone and in combination with Scr for prediction of AKI occurrence and death in AKI patients. (a) ROC curves for LDH prediction of AKI risk in hospitalized patients; (b) ROC curve of LDH combined with Scr for AKI risk prediction in hospitalized patients; (c) ROC curve of LDH for prediction of mortality risk in AKI patients; (d) ROC curve of LDH combined with Scr for prediction of mortality risk in AKI patients

图 2. LDH 单独及结合 Scr 预测 AKI 发生及 AKI 患者死亡的 ROC 曲线。(a) LDH 对住院患者 AKI 风险预测的 ROC 曲线；(b) LDH 联合 Scr 对住院患者 AKI 风险预测的 ROC 曲线；(c) LDH 对 AKI 患者死亡风险预测的 ROC 曲线；(d) LDH 联合 Scr 对 AKI 患者死亡风险预测的 ROC 曲线

4. 讨论

本研究首次探究了血清 LDH 水平与 AKI 发生风险及 AKI 患者住院全因死亡之间的关系。通过回顾性分析 4909 例患者的资料，比较不同血清 LDH 水平的住院患者的 AKI 发生率。结果显示，较高的 LDH 水平与住院患者的 AKI 发生风险及 AKI 患者死亡风险相关，LDH 水平是影响住院患者 AKI 发生及 AKI 患者死亡的独立危险因素。

人体内的 LDH 是一种酶类蛋白质，在细胞内负责催化乳酸的氧化反应，将乳酸转化为丙酮酸，同时还可逆转地将丙酮酸还原为乳酸[12] [17] [18]。LDH 广泛存在于机体的各种组织中，两个亚基 LDHA 和 LDHB 分别在骨骼肌和心肌中表达，其升高主要源于肺、肝脏和肌肉等组织的损伤[12]。LDH 在缺氧细胞的糖酵解代谢中起重要作用。在缺氧条件下，细胞无法依赖氧气来进行常规的细胞呼吸，因此转向糖酵解途径以产生能量。糖酵解途径增强产生的大量丙酮酸需要在细胞质中转化为乳酸，而这离不开的 LDH 催化作用[19] [20] [21]。一些研究认为当细胞坏死或凋亡时 LDH 被释放到血清中可作为组织损伤的生物标志物[22] [23]。研究表明，LDH 是许多疾病发生和进展的独立危险因素。Guan 等发现高 LDH 水平与心脏手术相关 AKI 的风险增加独立相关，并在临床实践中用于预测高风险患者[24]。血清 LDH 是一种经济有效的预后指标，可用于横纹肌溶解性 AKI 患者的危险分层[25]。有大量研究显示，LDH 水平升高 COVID-19 阳性住院患者发生 AKI 的独立危险因素，是细胞死亡和多器官衰竭的标志[26] [27] [28]。此外，

LDH 水平与急性胰腺炎、恶性肿瘤、COVID-19 的严重程度及预后有关[8] [29] [30] [31]。与之前的研究一致，本研究显示随着 LDH 水平的增加，AKI 发生率和 2~3 期比例也增加。

LDH 水平升高与 AKI 相关的确切机制可由以下因素部分解释。第一，具有大量线粒体的肾小管细胞易因缺氧而发生损伤[32]，诱导肾脏内的代谢组学发生变化，包括糖酵解和脂肪酸代谢的激活及线粒体功能障碍[33]。第二，LDH 是缺血性细胞损伤的重要反应因子，AKI 发生后肾小管细胞中的 LDH 表达水平快速增加[34]，LDH 从肾皮质释放到肾小囊腔和肾间质，最终到尿液和血液中[35]。第三，AKI 发生时的炎症反应可导致肾小管细胞的损伤，而损伤的肾小管细胞释放如肿瘤坏死因子-α 等炎症因子和单核细胞趋化蛋白-1 等趋化因子进一步加重炎症反应[36]。这导致肾小管细胞膜通透性升高，增加 LDH 释放，使血清 LDH 水平升高[35] [37] [38]。

此外，本研究还发现经模型校正后，血清 LDH 水平是 AKI 患者住院死亡的重要预测因素。与 Zhang 等人发现血清 LDH 水平与 AKI 危重患者院内死亡率相关的研究结果一致[16]。本研究发现 LDH 水平与 AKI 风险呈线性相关，AKI 的风险随着 LDH 水平升高而增加。因此应对 LDH 水平较高的患者进行更为积极的监测，并及时调整治疗策略。ROC 曲线分析显示 LDH 水平预测住院患者 AKI 的效能优于 Scr，为临床诊断 AKI 提供了参考价值。此外，当 LDH 和 Scr 联合预测 AKI 患者死亡风险时 AUC 增加至 0.80，较单一指标表现出更好的预测效能。

这项研究具有一些局限性。第一，本研究为单中心回顾性研究，没有对患者出院后随访，没有分析肾功能的长期变化及长期死亡率，在未来的研究中可以对出院患者进行随访作进一步分析。第二，患者尿量数据因记录过程主观因素准确性较低而未被纳入研究，可能会影响 AKI 的检出率。

5. 结论

血清 LDH 水平升高与住院患者发生 AKI 的风险独立相关，且较高水平的血清 LDH 与 AKI 患者住院死亡率增加相关。血清 LDH 可早期识别住院患者 AKI 风险，临床医师在工作中应重视监测患者血清 LDH 水平。

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