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· 临床研究 ·

非体外循环下冠脉搭桥术后急性肾损伤的危险因素及术前尿酸、白蛋白的预测价值分析*

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摘要 目的:探讨非体外循环下冠脉搭桥术(OPCAB)后急性肾损伤(AKI)的危险因素,并分析术前尿酸(UA)、白蛋白(ALB)对OPCAB术后AKI的预测价值。**方法:**纳入我院2018年5月~2020年5月收治的134例行OPCAB术的冠心病患者,收集其临床资料。术后观察48h,根据患者是否发生AKI分成AKI组和非AKI组,分析患者OPCAB术后AKI发生的影响因素,绘制受试者工作特征(ROC)曲线分析术前血清UA、ALB对OPCAB术后AKI的预测价值。**结果:**在134例患者中,有37例患者行OPCAB术后发生AKI,发生率为27.61%(37/134)。单因素分析结果显示,AKI组年龄≥65岁、高血压史、糖尿病史、术前心功能IV级人数占比和术前血清UA较非AKI组升高,而术前血清ALB较非AKI组降低($P<0.05$)。多因素Logistic回归分析结果显示,年龄≥65岁、高血压史、糖尿病史、术前心功能IV级、术前血清UA≥350.71 μmol/L是术后发生AKI的危险因素,而术前血清ALB≥39.22 g/L是AKI的保护因素($P<0.05$)。术前血清UA、ALB及二者联合预测OPCAB术后AKI发生的曲线下面积(AUC)分别为0.771、0.722、0.881。**结论:**OPCAB术后AKI发生率较高,AKI主要与患者年龄、高血压史、糖尿病史、术前心功能分级以及术前血清UA、ALB水平有关,其中术前血清UA、ALB对AKI发生有一定预测价值,临床可通过测定术前UA、ALB水平,辅助评估OPCAB术后AKI的发生风险。

关键词:非体外循环;冠脉搭桥术;急性肾损伤;尿酸;白蛋白;危险因素;预测价值

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Risk Factors of Acute Kidney Injury after Off-pump Coronary Artery Bypass Grafting and the Predictive Value of Preoperative Uric Acid and Albumin*

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ABSTRACT Objective: To investigate the risk factors of acute kidney injury (AKI) after off-pump coronary artery bypass grafting (OPCAB), and analyze the predictive value of preoperative uric acid (UA) and albumin (ALB) in OPCAB postoperative AKI. **Methods:** 134 patients with coronary heart disease who underwent OPCAB in our hospital from May 2018 to May 2020 were included, and their clinical data were collected. Postoperative observation was performed for 48h, according to whether the patients had AKI, they were divided into AKI group and non-AKI group, the influencing factors in patients with OPCAB postoperative AKI were analyzed. Receiver operating characteristic (ROC) curve was drawn to analyze the predictive value of preoperative serum UA and ALB for OPCAB postoperative AKI. **Results:** Among 134 patients, AKI occurred in 37 patients after OPCAB, with an incidence of 27.61%(37/134). Univariate analysis showed that age ≥ 65 years old, hypertension history, diabetes history, preoperative heart function grade IV accounted and preoperative serum UA in AKI group were significantly higher than those in the non-AKI group, while the preoperative serum ALB was lower than that in the non-AKI group ($P<0.05$). Multiivariable Logistic regression analysis showed that age ≥ 65 years old, hypertension history, diabetes history, preoperative heart function grade IV and preoperative serum UA ≥ 350.71 μmol/L were risk factors for postoperative AKI occurred, and preoperative serum ALB ≥ 39.22g/L was a protective factor for AKI ($P<0.05$). The area under the curve (AUC) of preoperative serum UA, ALB and their combination in predicting OPCAB postoperative AKI were 0.771, 0.722 and 0.881, respectively. **Conclusion:** The incidence rate of OPCAB postoperative AKI is higher, and AKI is mainly related to the patient's age, hypertension history, diabetes history, preoperative heart function grade and preoperative serum UA and ALB. The preoperative serum UA and ALB have certain predictive value for the AKI occurred, the preoperative level of both can be measured clinically, so they can

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auxiliary evaluate the risk of OPCAB postoperative AKI.

Key words: Off-pump; Coronary artery bypass graft; Acute kidney injury; Uric acid; Albumin; Risk factors; Predictive value

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前言

非体外循环下冠脉搭桥术(Off-pump coronary artery bypass grafting, OPCAB)在冠心病治疗中应用较广泛,与传统手术相比,OPCAB术能够减少对肺功能、心功能等重要脏器的影响,安全性相对较高。然而,患者术后仍不能完全避免并发症的发生,其常见的危重并发症为急性肾损伤(Acute kidney injury, AKI)^[1]。OPCAB术后AKI的相关病因主要包括肾性因素、肾前性因素两种类型,前者是指因各种因素诱发的肾缺血、肾中毒,后者是指因各种原因导致的有效循环血量下降,肾脏灌注压下调,肾小球滤过率降低,但肾实质完整性未受损^[2]。既往研究表明OPCAB术后AKI发生率约为30%,即便患者仅出现轻微的血肌酐(Serum creatinine, Scr)升高,也可能导致预后不良,危害性极大,严重情况下会进展成慢性肾衰竭、终末期肾病,危及患者生命^[3],因此,尽早明确OPCAB术后AKI发生的危险因素,预测AKI发生风险很有必要。目前研究^[4]大多局限于分析OPCAB术对患者肾功能的影响,尚未寻求到理想指标对AKI发生进行预测。炎症参与了AKI进展过程,炎症介质可引起内皮损伤、血管舒缩紊乱等病变,诱发肾血流动力学异常^[5],而白蛋白(Albumin, ALB)具备减轻炎症、促进微循环改善的作用^[6],尿酸(Uric acid, UA)则属于促炎介质,可促进炎性因子合成与释放^[7],但尚不明确二者是否能作为预测OPCAB术后AKI的指标。基于此,本研究纳入134例行OPCAB术的冠心病患者进行分析,观察术后AKI发生的危险因素及分析术前血清UA、ALB对AKI发生的预测价值,以期为临床OPCAB术后AKI风险评估提供参考,现报告如下。

1 资料与方法

1.1 一般资料

纳入我院2018年5月~2020年5月收治的134例行OPCAB术的冠心病患者,其中男88例,女46例,年龄40~75岁,平均(58.35 ± 14.42)岁;体质质量指数18~25 kg/m²,平均(22.34 ± 1.53)kg/m²;基础疾病:高血压28例,糖尿病34例,高脂血症29例;心功能分级:I级42例,II级45例,III级36例,IV级11例。

1.2 纳入、排除标准

纳入标准:(1)经冠状动脉造影或超声心动图检查,证实为冠心病;(2)年龄>18岁;(3)无法行介入术,或介入治疗失败;(4)具备OPCAB术指征,择期完成手术;(5)术前未出现肾损伤;(6)病例资料完整。排除标准:(1)术前需行肾代替治疗者;(2)同期需行肾脏手术者;(3)恶性肿瘤者;(4)凝血功能异常者;(5)既往有泌尿系统病史者;(6)脑、肝、肺等其它重要脏器严重受损者;(7)术前使用过影响血清UA、ALB水平的药物者,如嘌呤醇、白蛋白注射液等。

1.3 手术方法

(1)术前准备:患者术前行常规超声心动图、肝肾功能、凝血功能、血常规等检查。根据患者血常规检查结果纠正贫血,根据超声心动图检查结果使用预防心房颤动药物。(2)手术操作:所有患者均行OPCAB术。术前行全身麻醉,于胸骨正中做切口,取大隐静脉、左乳内动脉,在左乳内动脉断开之前,取1~1.5 mg/kg 肝素(常州千红生化制药股份有限公司,国药准字H32022088,规格:2 mL:12500单位)静注,全血激活凝固时间控制为200~400s,每间隔30 min 观察1次。将心包切开,并进行悬吊,使心脏显露,对升主动脉进行探查,观察是否存在钙化斑块,并确定病变冠脉,明确靶血管吻合口的具体位置。先对前降支、乳内动脉行吻合,以便提升心脏抗搬运耐受力,然后按照冠脉病变情况,依次针对对角支、右冠(或分支)、回旋支(或分支)进行吻合。在吻合过程中,必须确保吻合一支,并开放一支,使心肌血供满意,提升心脏耐受性。待桥血管吻合完毕,经美国Transonic T400超声血流仪对桥血管血流量进行检测,评估通畅程度,若血流量不足5 mL/min,则需重新进行搭桥。检查吻合口的出血情况,确定无出血后,安装心脏临时起搏导线,针对局部组织行间断缝合,操作时对桥血管进行保护。安置心包,并置入纵膈引流管,关胸。(3)术后处理:术后给予扩张血管、抗炎、胃黏膜保护、祛痰止咳等处理。针对术后血压较低的患者,及时对血容量进行补充,给予维持血压治疗,尿量保持在1~3 mL/(kg·h),必要情况下给予利尿剂。密切观察患者动脉血气、电解质变化情况,确保内环境稳定,若发生少尿现象,则需补钾,若尿量持续低于0.5 mL/(kg·h),甚至无尿,则实施肾脏替代治疗。

1.4 观察指标

(1)记录AKI发生情况:根据患者术后48 h是否发生AKI分成AKI组和非AKI组。AKI诊断^[8]:术后48 h内Scr升高 $\geq 26.5 \mu\text{mol/L}$,或与基础值相比升高 $\geq 50\%$,或者尿量低于0.5 mL·kg⁻¹·h⁻¹,持续时间超过6 h。参考全球肾病预后组织(Kidneydisease: improving global outcomes organization, KDIGO)分期标准^[9]进行分期:1期:Scr为基线值的1.5~1.9倍,或者Scr升高 $\geq 26.5 \mu\text{mol/L}$,或者尿量连续6~12 h低于0.5 mL·kg⁻¹·h⁻¹;2期:Scr为基线值的2.0~2.9倍,或者尿量连续超过12 h低于0.5 mL·kg⁻¹·h⁻¹;3期:Scr为基线值的3倍或更高,或者尿量连续超过24 h低于0.3 mL·kg⁻¹·h⁻¹,或超过12 h无尿。

(2)临床资料收集:通过体格检查、查看病例资料等方式,收集患者临床资料,包括性别、年龄、体质质量指数、高血压史、高脂血症史、糖尿病史、术前心功能分级、机械通气时间、ICU住院时间、术前左室射血分数(Left ventricular ejection fraction, LVEF)、术前血清Scr、UA、ALB、术中出血量、术中输血、术中使用血管活性药物、术后发热情况。(3)血清指标检测:于患者术前采集3 mL空腹静脉血,行离心处理,转速3000 r/min,离心半径11.5 cm,时间为20 min,分离血清,保存于低温冰箱(-70°C)待测。采用过氧化物酶法测定血清UA水平,试剂盒购自深圳迈瑞生物医疗有限公司。经免疫比浊法测定血清ALB

水平,试剂盒购自深圳市生科源技术有限公司。经终点法测定Scr水平,试剂盒购自上海北海生物技术工程有限公司。LVEF经超声心动图(武汉迈新医疗设备有限责任公司,DC-25彩色多普勒超声)测定。

1.5 统计学方法

经SPSS20.0软件行数据分析。计数资料用百分比(%)表示,行 χ^2 检验。计量资料以均数±标准差($\bar{x} \pm s$)表示,行t检验。等级资料行秩和检验。经单因素及多因素Logistic回归分析OPCAB术后AKI发生的影响因素。绘制受试者工作特征(Receiver operating characteristic,ROC)曲线分析术前血清UA、ALB对OPCAB术后AKI发生的预测价值,明确曲线下面积(Area under curve,AUC)。 $P < 0.05$ 为差异有统计学意义。

2 结果

表1 患者术后AKI影响因素的单因素分析

Table 1 Single factor analysis of influencing factors of postoperative AKI

Factors	n	AKI group(n=37)	Non-AKI group(n=97)	t/ χ^2/U	P
Gender(n)	Male	88	26(70.27%)	62(63.92%)	0.480
	Female	46	11(29.73%)	35(36.08%)	0.489
Age(years)	≥ 65	55	24(64.86%)	31(31.96%)	11.985
	<65	79	13(35.14%)	66(68.04%)	0.001
Body mass index(kg/m ²)	≥ 24	29	10(27.03%)	19(19.59%)	0.874
	<24	105	27(72.97%)	78(80.41%)	0.350
Hypertension history(n)	Yes	28	15(40.54%)	13(13.40%)	11.934
	No	106	22(59.46%)	84(86.60%)	0.001
Hyperlipidemia history(n)	Yes	29	11(29.73%)	18(18.56%)	1.972
	No	105	26(70.27%)	79(81.44%)	0.160
Diabetes history(n)	Yes	34	19(51.35%)	15(15.46%)	18.217
	No	100	18(48.65%)	82(84.54%)	0.000
Preoperative heart function grade(n)	I grade	42	13(35.14%)	29(29.90%)	9.760
	II grade	45	11(29.73%)	34(35.05%)	0.021
	III grade	36	6(16.22%)	30(30.93%)	
	IV grade	11	7(18.92%)	4(4.12%)	
Mechanical ventilation time(h)		30.15±6.71	28.46±5.63	1.471	0.144
Length of stay in ICU(d)		3.23±0.45	3.11±0.38	1.551	0.123
Preoperative LVEF(%)		46.29±6.64	48.43±5.34	1.935	0.055
Preoperative Scr(μmol/L)		69.81±8.96	65.93±10.65	1.965	0.052
Preoperative serum UA(μmol/L)		476.43±89.79	302.75±56.68	13.347	0.000
Preoperative serum ALB(g/L)		27.54±4.43	43.68±7.79	11.874	0.000
Intraoperative blood loss(ml)		612.49±65.48	605.89±44.12	0.672	0.503
Intraoperative blood transfusion(n)	Yes	21	8(21.62%)	13(13.40%)	1.369
	No	113	29(78.38%)	84(86.60%)	0.242
Vasoactive drugs were used during the operation(n)	Yes	26	10(27.03%)	16(16.49%)	1.900
	No	108	27(72.97%)	81(83.51%)	0.168
Postoperative fever(n)	Yes	15	6(16.22%)	9(9.28%)	1.297
	No	119	31(83.78%)	88(90.72%)	0.255

2.1 患者术后AKI发生情况

134例患者中,有37(27.61%)例术后发生AKI,97(72.39%)例未发生AKI。在37例AKI患者中,KDIGO1期20(54.05%)例,2期11(29.73%)例,3期6(16.22%)例。其中1期、2期患者均经治疗后出院,无死亡病例,3期患者有2例死亡,其余患者均行肾替代治疗。

2.2 患者术后AKI影响因素的单因素分析

AKI组年龄≥65岁、高血压史、糖尿病史、术前心功能Ⅳ级人数占比高于非AKI组,且AKI组术前血清UA高于非AKI组,术前血清ALB低于非AKI组($P < 0.05$)。两组在性别、体质指数、高脂血症史、机械通气时间、ICU住院时间、术前LVEF、术前Scr、术中出血量、术中输血、术中使用血管活性药物、术后发热方面比较无明显差异($P > 0.05$),见表1。

2.3 患者术后 AKI 影响因素的多因素 Logistic 回归分析

术前血清 UA、ALB 以均数为界赋值,以年龄、高血压史、糖尿病史、术前心功能分级及术前血清 UA、ALB 为自变量 X, 以术后是否发生 AKI 为因变量 Y(未发生=0,发生=1),纳入

多因素 Logistic 回归模型。结果显示,年龄 ≥ 65 岁、高血历史、糖尿病史、术前心功能IV级、术前血清 UA $\geq 350.71 \mu\text{mol/L}$ 是术后发生 AKI 的危险因素,而术前血清 ALB $\geq 39.22 \text{ g/L}$ 是 AKI 的保护因素($P<0.05$),见表 2。

表 2 患者术后 AKI 影响因素的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis of influencing factors of postoperative AKI in patients

Variable	Quantitative assignment	B	SE	χ^2	P	OR	95%CI
Age	<65 years old=0, ≥ 65 years old=1	1.602	0.474	11.439	0.000	4.961	1.961-12.550
Hypertension history	No=0, Yes=1	1.129	0.333	11.507	0.000	3.094	1.611-5.942
Diabetes history	No=0, Yes=1	1.405	0.323	18.853	0.000	4.074	2.161-7.680
Preoperative heart function grade	I grade=0, II grade=1, III grade=2, IV grade=3						
	I grade	1.259	0.833	2.284	0.131	3.522	0.688-18.030
	II grade	1.385	0.811	2.921	0.087	3.996	0.816-19.569
	III grade	1.087	0.602	3.259	0.071	2.965	0.911-9.650
	IV grade	1.288	0.409	9.897	0.002	3.625	1.625-8.087
Preoperative serum UA	<350.71 $\mu\text{mol/L}$ =0, $\geq 350.71 \mu\text{mol/L}$ =1	1.268	0.347	13.380	0.000	3.552	1.801-7.005
Preoperative serum ALB	<39.22 g/L=0, $\geq 39.22 \text{ g/L}$ =1	-0.145	0.044	11.015	0.000	0.865	0.794-0.942

2.4 术前血清 UA、ALB 对 OPCAB 术后 AKI 发生的预测价值分析

术前血清 UA、ALB 预测 OPCAB 术后 AKI 发生的 AUC

分别为 0.771、0.722, 二者联合预测的 AUC 为 0.881, 见表 3, ROC 曲线见图 1。

表 3 术前血清 UA、ALB 对 OPCAB 术后 AKI 发生的预测价值分析

Table 3 Analysis of the predictive value of preoperative serum UA and ALB for OPCAB postoperative AKI occurred

Indexes	AUC	Standard error	P	95%CI	Optimal boundary value	Sensitivity(%)	Specificity(%)
Preoperative serum UA ($\mu\text{mol/L}$)	0.771	0.047	0.000	0.679-0.862	400.225	67.60	70.10
Preoperative serum ALB(g/L)	0.722	0.052	0.000	0.621-0.823	34.935	78.40	40.20
Preoperative serum UA combined with ALB	0.881	0.37	0.000	0.808-0.954	--	86.50	89.70

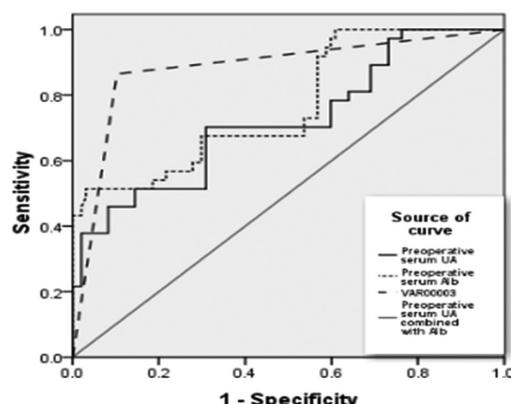


图 1 术前血清 UA、ALB 预测 OPCAB 术后 AKI 发生的 ROC 曲线
Fig.1 ROC curve of preoperative serum UA and ALB predicting OPCAB postoperative AKI occurred

3 讨论

AKI 是 OPCAB 术后比较常见的一种并发症,其发生机制较复杂,临床认为炎症、氧化应激等因素参与了 AKI 进展过程,这些因素可导致患者肾小管细胞损害,部分细胞受损后能够恢复,但部分细胞凋亡,可引起肾损伤,增加术后 AKI 发生风险^[10]。急性肾脏缺血性损害属于低灌注损伤,当这种损伤导致肾脏调节功能被破坏时,肾脏功能易受低灌注影响,在手术后出现肌酐升高、尿量减少等表现,诱发 AKI^[11]。若未能及时救治,则会导致肾小管进一步受损,进展成肾性 AKI,增加死亡风险^[12]。临床亟需通过明确 OPCAB 术后 AKI 发生的危险因素,寻求理想指标对其进行预测,以便及时了解 AKI 发生风险,给予针对性处理,改善预后。

研究表明,心脏手术患者术后血流动力学稳定性欠佳,因心室功能损害,容易引起心输出量减低、肾灌注损害等并发症^[13,14]。此外,手术过程中麻醉药物的使用可能削弱机体自动调节功能,致围术期出现肾脏缺血,引起肾灌注损害,再加上手术创伤能促进炎症因子释放,可引起炎症、氧化应激等表现,增加术后AKI发生风险^[15,16]。本结果显示,在134例行OPCAB术的患者中,AKI发生率约为27.61%。孙晴等^[17]研究提示,OPCAB术后AKI发生率为22.77%,与本次结论接近。本研究发现年龄≥65岁的患者OPCAB术后AKI发生风险明显升高,分析原因,可能在于年龄越大的患者,机体功能下降越明显,合并基础疾病越多,随着年龄增长,血管脆性增加,更容易诱发微栓肾动脉栓塞,引起术后AKI^[18]。心脏供血与患者手术耐受性、年龄密切相关,但患者年龄越大,心脏供血能力越差,局部功能削弱,手术耐受性欠佳,其因心脏手术造成的器官衰竭发生率也随之升高^[19]。基于此,临床针对这类患者要对其机体状况进行全面评估,术前做好充分的准备工作,根据情况预防性用药,控制术后AKI发生风险。

本次结果提示,高血压史、糖尿病史是患者术后AKI发生的危险因素。高血压是老年人中的常见病,手术应激引起的血压变化可激活患者肾素-血管紧张素-醛固酮系统,促进肾血管收缩,影响局部血液供应,诱发肾缺血,导致肾衰竭^[20,21]。血压变化还可能导致血液内红细胞功能不稳定,激活凝血系统,大量消耗凝血因子,继而引起纤溶系统亢进,削弱肾微血管功能,增加肾损伤风险^[22]。糖尿病诱发AKI的机制可能在于,血糖波动会导致血管产生剧烈改变,引起血管血流量异常,而肾脏极易受血管血流量异常影响,导致其功能受损,具体表现为肾小球缺氧以及缺血,诱发AKI^[23]。因此,在手术实施前,临床需对合并高血压、糖尿病的患者积极进行控压、控糖处理,使血压、血糖恢复至正常范围,并在围术期加强监控,密切监测相关指标的变化,为机体恢复提供良好的内环境。本研究显示,术前心功能IV级是患者术后AKI发生的危险因素。研究发现,若患者心功能太差,在行心脏手术后一段时间内,可能出现明显的心排量减低,有效血液循环也明显下降,以肾脏反应最敏感,在这种情况下,肾脏血供不足,容易诱发肾缺氧,还可导致肾脏炎症^[24,25]。鉴于此,在手术实施前,临床针对心功能较差的患者,需给予针对性药物干预,尽可能提升心功能。

本结果显示,术前血清UA350.71 μmol/L会增加患者术后AKI发生风险,而术前血清ALB≥39.22 g/L则对术后AKI发生存在预防作用,且最终证实二者对AKI发生存在一定预测价值,AUC均大于0.720。UA实际上属于促炎介质,对C反应蛋白表达有诱导作用,能促进单核细胞趋化蛋白-1产生,其还能促进血管平滑肌细胞增殖,诱发氧化应激,导致内皮细胞损害,该机制可引起肾小球硬化,增加AKI发生风险^[26,27]。此外,当UA滤过量高于肾小管重吸收能力后,尿液内尿酸盐含量升高,一旦形成结晶则可使肾小管受堵,降低肾血流量,下调肾小球滤过率,诱发AKI^[28]。ALB则具有促进氧自由基清除、抗血栓等生物功能,其预防AKI的机制可能在于,它能与肾毒性物质结合,减轻肾毒性,此外,其还能与一氧化氮结合,产生S-亚硝基-白蛋白,有利于维持肾灌注,预防肾小球滤过率减低^[29]。因此,临床需密切观察患者术前血清UA、ALB的变化,及时对

UA水平升高进行抑制,并避免ALB水平过低,降低术后AKI发生率。林倩等^[30]发现术前高UA血症会增加心脏手术后AKI发生风险,为本次结论给予了支持,但该研究仅能体现UA与AKI发生的关系,而本研究一方面明确了AKI的危险因素,并且探讨了术前血清UA、ALB对OPCAB术后AKI的预测价值,临床可考虑将二者作为评估AKI风险的重要指标。

综上所述,OPCAB术后AKI发生与患者年龄、高血史、糖尿病史、术前心功能分级、术前血清UA、ALB存在关联,尤其术前血清UA、ALB检测对预测AKI发生风险有一定价值。

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