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经内镜逆行胰胆管造影术后急性胰腺炎患者的血浆白蛋白水平的变化与预后的相关性 *

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摘要 目的:探讨经内镜逆行胰胆管造影术前后急性胰腺炎患者的血浆白蛋白水平的变化与预后的相关性。**方法**:2015 年 8 月到 2019 年 1 月选择在本院诊治的急性胰腺炎患者 68 例，根据治疗方法的不同分为经内镜逆行胰胆管造影 (encoscopic retrograde cholangio pancreatography,ERCP)组和保守治疗组,同期选择在本院进行体检的非胰腺炎患者 34 例作为对照组。ERCP 组患者都给予经内镜逆行胰胆管造影手术治疗,保守治疗组给予内科保守治疗。记录血浆白蛋白水平变化情况,及预后并进行相关性分析。**结果**:ERCP 组和保守治疗组入院时的白细胞计数、中性粒细胞计数、C- 反应蛋白、降钙素原均显著高于对照组,淋巴细胞计数、白蛋白均显著低于对照组(P<0.05),且上述指标 ERCP 组和保守治疗组变化无统计学意义 (P>0.05)。在 ERCP 组和保守治疗组中,术后 1 d 血浆白蛋白水平低于术前 1 d(P<0.05),但是术后 3 d、术后 7 d 显著高于术前 1 d,且 ERCP 组术后术后 3 d、术后 7 d 血浆白蛋白水平显著高于保守治疗组 (P<0.05)。在 ERCP 组治疗的总有效率显著高于保守治疗组(P<0.05);两组并发症发生率对比无统计学意义(P>0.05)。在 ERCP 组中,选取白蛋白、降钙素原水平等因素,通过 logistic 回归分析证实白蛋白、降钙素原为影响患者预后的主要危险因素(P<0.05)。**结论**:急性胰腺炎患者经内镜逆行胰胆管造影手术前后血浆白蛋白水平有显著波动,白蛋白、降钙素原与患者预后显著相关,可预测患者的预后。

关键词:急性胰腺炎;经内镜逆行胰胆管造影手术;白蛋白;预后;相关性

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Changes of Plasma Albumin Levels in Patients with Acute Pancreatitis after Endoscopic Retrograde Cholangiopancreatography Correlation with Prognosis*

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ABSTRACT Objective: To investigate the correlation between the changes of plasma albumin levels and prognosis in patients with acute pancreatitis before and after pancreatic surgery. **Methods:** From August 2015 to January 2019, 68 patients with acute pancreatitis who were treated in our hospital from August 2015 to January 2019 were divided into two groups: endoscopic retrograde cholangio pancreatography (ERCP) group and conservative treatment group. In the same period, 34 patients with non-pancreatitis who underwent physical examination in our hospital were selected as the control group. Patients in the ERCP group were treated with endoscopic retrograde cholangiopancreatography, and the conservative treatment group received conservative medical treatment. Record changes in plasma albumin levels, prognosis and correlation analysis. **Results:** The white blood cell count, neutrophil count, C-reactive protein and procalcitonin were significantly higher in the ERCP group and the conservative treatment group than in the control group. The lymphocyte count and albumin were significantly lower than the control group (P<0.05). There was no significant difference in the above indicators between the ERCP group and the conservative treatment group (P>0.05). In the ERCP group and the conservative treatment group, plasma albumin levels were lower than 1 day before operation (P<0.05), but significantly higher than 3 days after surgery and 1 day after surgery, and ERCP group. Plasma albumin levels were significantly higher after 3 days and 7 days after surgery (P<0.05). The total effective rate of treatment in the ERCP group was significantly higher than that in the conservative treatment group (P<0.05). There was no significant difference in the incidence of complications between the two groups (P>0.05). In the ERCP group, factors such as albumin and procalcitonin were selected. Logistic regression analysis confirmed that albumin and procalcitonin were the main risk factors for prognosis (P<0.05). **Conclusion:** Patients with acute pancreatitis have significant fluctuations in plasma albumin levels before and after endoscopic retrograde cholangiopancreatography. Albumin and procalcitonin are significantly associated with prognosis and predict prognosis.

Key words: Acute pancreatitis; Endoscopic retrograde cholangiopancreatography; Albumin; Prognosis; Correlation

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前言

急性胰腺炎(acute pancreatitis,AP)是一种非常凶险的急腹症,其是由多种病因导致胰腺内胰酶被异常激活后引起的胰腺组织自身水肿、出血、坏死的炎症反应,表现出发热、上腹痛、呕吐和血清淀粉酶升高等[1,2]。当前急性胰腺炎的发病机制没有统一的说法,可能与"瀑布效应"、胰腺自身消化等有关[3];病因包括胆道系统疾病、慢性胰腺炎、酗酒、自身免疫性损伤等[4,5]。近年来,手术治疗该病取得了比较好的效果,其中经内镜逆行胰胆管造影(encoscopic retrograde cholangio pancreatography,ERCP)具有微创、操作简单与安全等优势。但也会出现一定的术后并发症[6]。如术后早期可出现营养不良,腹痛、腹胀、感染等[7,8]。目前用于判定该病患者预后的评分系统包括 APACHEⅡ评分、CT 评分等,但这些评分系统都有很高的假阳性率,且较为复杂、繁琐,并不被临床医生经常使用[9,10]。有研究显示血浆白蛋白水平下降可增加胃肠切除术后的特定并发症发生率,低蛋白血症是手术后并发症的独立危险因素[11,12],但是在胰腺手术中的应用还无相关报道。本文具体探讨了胰腺手术前后血浆白蛋白水平的变化与预后的相关性,以明确白蛋白的预测价值。现总结报道如下。

1 资料与方法

1.1 一般资料

2015 年 8 月至 2019 年 1 月选择在本院诊治的急性胰腺炎患者 68 例作为病例组,都符合急性胰腺炎的诊断标准(血清淀粉酶或脂肪酶超过 3 倍的正常参考范围上限;影像学检查发现胰腺水肿或坏死),患者出现胰腺局部并发症或产生压迫症状,或无症状但胰腺及胰周出现无菌性坏死积液时进行手术治疗。根据治疗的方法分为 ERCP 组和保守治疗组,各 34 例,同期选择在本院进行体检的非胰腺炎患者 34 例作为对照组。纳入标准:医院伦理委员会批准了此次研究;患者签署了知情同意书;病例组患者发病 24 h 内就诊。排除标准:严重心、脑、肝病等其他重要脏器疾病患者;临床资料缺乏者;胰腺癌等其他胰胆系统疾病者。

ERCP 组中 24 例,女 10 例,平均年龄 53.42± 2.32 岁;平均体重指数 23.65± 2.35 kg/m^2;平均发病到入院时间 11.52± 0.37 h;平均 APACHEⅡ评分 8.75± 0.42 分;平均 RANSON 评分 4.68± 0.34 分;平均 CT 评分 3.04± 0.21 分。

保守治疗组中男 26 例,女 8 例;平均年龄 55.30± 2.48 岁;平均体重指数 23.94± 2.43 kg/m^2;平均发病到入院时间 13.19± 0.49 h;平均 APACHEⅡ评分 8.92± 0.49 分;平均 RANSON 评分 4.83± 0.44 分;平均 CT 评分 3.09± 0.29 分。

对照组中男 25 例,女 9 例;平均年龄 54.52± 3.13 岁;平均体重指数 22.83± 1.82 kg/m^2。三组的一般资料对比具有可比性(P>0.05)。

1.2 治疗方法

ERCP 组和保守治疗组在发病后 1~7 d 内治疗,均给予禁食、胃肠减压、应用抗生素、抑制胰酶和胃酸分泌等常规治疗。

ERCP 组:术前 1 h 开始静脉注射抗生素和镇静剂、解痉剂,选择 Pentax-34H 型十二指肠镜,均由同一组有经验多内镜医生和护士共同参与完成,机械碎石网蓝、取石网蓝、气囊导管,行氧饱和和心电监护,尽量使胆、胰管分别显影并控制显影的次数(<3 次)和造影剂剂量(显影能明确诊断即可)、常规左侧卧位、俯卧位、仰卧位、右侧卧位摄片。术后禁食 24~72 h。

保守治疗组:给予内科保守治疗。针对炎症反应的早期处理包括皮质激素和抗生素进行积极的抗感染治疗。

1.3 血浆白蛋白检测

(1)检测 ERCP 组和保守治疗组患者在入院时、术后 1 d、术后 3 d、术后 7 d 与对照组患者入院时的血浆白蛋白(albumin,ALB)水平。(2)同时检测三组患者入院时的白细胞计数、中性粒细胞计数、淋巴细胞计数、C- 反应蛋白、降钙素原水平。(3)记录 ERCP 组和保守治疗组的预后情况,包括术后 14 d 的疗效与并发症发生情况,疗效标准:显效:腹痛、腹胀、恶心、呕吐等肠道功能恢复;有效:腹痛、腹胀等肠道功能部分恢复;无效:腹痛、腹胀等肠道功能无改变或加重。总有效率=(显效 + 有效)/组内例数× 100.0%。并发症包括胰瘘、胃排空延迟、出血、感染等。

1.4 统计方法

选择 SPSS19.00,计量资料用($\bar{x}\pm s$)表示,计数数据%表示,采用 x^2 检验与 t 检验等,相关性分析采用 logistic 回归分析,统计学有意义的标准为 P<0.05。

2 结果

2.1 常规血液学指标对比

ERCP 组和保守治疗组入院时的白细胞计数、中性粒细胞计数、C- 反应蛋白、降钙素原均显著高于对照组,淋巴细胞计数、白蛋白均显著低于对照组(P<0.05),且上述指标 ERCP 组和保守治疗组变化无统计学意义 (P>0.05)。见表 1。

表 1 三组常规血液学指标对比($\bar{x}\pm s$)

Table 1 Comparison of routine hematological indicators among the three groups ($\bar{x}\pm s$)

Groups	n	Leucocyte count (× 10^9/L)	Neutrophil count (× 10^9/L)	Lymphocyte count (× 10^9/L)	CRP (mg/L)	Calmodulin (μg/L)	Albumin (g/L)
ERCP group	34	15.65± 2.13*	9.45± 2.10*#	1.39± 0.11*	78.20± 11.09*	3.47± 0.33*	115.36± 22.12*
Conservative treatment group	34	15.14± 2.25*	9.36± 2.21*	1.37± 0.14*	78.43± 11.15*	3.42± 0.35*	115.62± 21.44*
Control group	34	5.72± 1.01	3.52± 0.44	1.99± 0.32	4.10± 0.22	0.03± 0.01	154.63± 21.96

Note: compared with the control group, *P<0.05, compared with the conservative treatment group, #P<0.05.

2.2 血浆白蛋白变化对比

在 ERCP 组和保守治疗组中，术后 1 d 血浆白蛋白水平低于术前 1 d(P<0.05)，但是术后 3 d、术后 7 d 显著高于术前 1 d，且 ERCP 组术后术后 3 d、术后 7 d 血浆白蛋白水平显著高于保守治疗组 (P<0.05)。见表 2。

表 2 ERCP 组和保守治疗组手术前后血浆白蛋白变化对比 (g/L, $\bar{x}\pm s$)

Table 2 Comparison of plasma albumin changes before and after surgery in ERCP group and conservative treatment group (g/L, $\bar{x}\pm s$)

Groups	Time point	n	Albumin (g/L)
ERCP group	Preoperative 1 d	34	115.36± 22.12
	Postoperative 1 d	34	100.32± 33.10*
	Postoperative 3 d	34	163.52± 25.88*#
	Postoperative 7 d	34	191.52± 20.85*#
	F		90.357
	P		0.000
Conservative treatment group	Preoperative 1 d	34	115.62± 21.44
	Postoperative 1 d	34	90.78± 21.35*
	Postoperative 3 d	34	125.25± 22.21*
	Postoperative 7 d	34	158.59± 34.23*
	F		41.522
	P		0.000

Note: compared with the preoperative 1 d, *P＜0.05; compared with the conservative treatment group, #P＜0.05.

2.3 预后情况

在 ERCP 组治疗的总有效率显著高于保守治疗组(P<0.05)见表 3；两组并发症发生率对比无统计学意义(P>0.05)，见表 4。

表 3 ERCP 组和保守治疗组治疗效率对比(例，%)

Table 3 Comparison of treatment efficiency of ERCP group and conservative treatment group (n,%)

Groups	n	Excellence	Effective	Invalid	Total efficiency
ERCP group	34	25	6	3	31(91.2)*
Conservative treatment group	34	18	5	11	23 (67.6)

表 4 ERCP 组和保守治疗组的并发症的对比(例，%)

Table 4 Comparison of complications between ERCP group and conservative treatment group (n, %)

Groups	n	Pancreatic fistula	Delayed gastric emptying	Haemorrhage	Infect	Total
ERCP group	34	1	1	1	1	4 (11.8)
Conservative treatment group	34	3	2	0	0	5 (14.7)

Note: compared with the conservative treatment group, *P＜0.05.

2.4 相关性分析

在 ERCP 组中，选取白蛋白、降钙素原水平等因素，通过 logistic 回归分析证实白蛋白、降钙素原为影响患者预后的主要危险因素(P<0.05)。见表 5。

表 5 影响病例组患者预后的相关因素分析(n=68)

Table 5 Analysis of factors related to prognosis in patients in the case group (n=68)

Index	β	SE	Wald	*P*	OR	95%CI
Albumin	3.879	0.789	20.778	0.000	2.752	1.772-10.832
Calmodulin	2.190	0.914	17.179	0.000	1.066	1.003-8.814

3 讨论

急性胰腺炎是全身炎症反应综合征，大量蛋白质被分解，患者机体处于持续高代谢状态，伴随有水电解质紊乱，存在严重的负氮平衡[13,14]。并且由于胰腺位于腹膜后，位置较深，使得胰腺炎的早期症状不明显且无特征性，在就诊时已处于急性期，需要进行急诊手术治疗。并且该病的保守治疗效果不佳[15,16]。患者存在较多渗液时，如不积极进行手术引流，则大量细胞因子、炎性递质可引发瀑布效应，导致死亡[17]。同时采用创伤较大的开腹手术会加重对机体的负担，加重全身应激反应，不利于预后改善[18]。经内镜逆行胰胆管造影手术是临床上被广泛应用诊治胰胆系统疾病的重要治疗手段，属于微创术，与外科手术效果相同[19]。本研究在 ERCP 组治疗的总有效率显著高于保守治疗组；两组并发症发生率对比无统计学意义，表明经内镜逆行胰胆管造影手术对于急性胰腺炎具有很好的治疗效果。

急性胰腺炎的病变程度轻重不等，轻者病情常呈自限性，但是疾病危重者可引发胰腺局部炎症反应，伴有其他器官功能损害的疾病，有比较高的病死率[20,21]。特别是在疾病进展后期，胰腺及周围组织坏死伴发感染，将进一步加重急性胰腺炎的严重程度。一些反映炎症指标与常规生化指标也被应用于判定急性胰腺炎患者的预后，包括白细胞计数、中性粒细胞计数、淋巴细胞计数、C- 反应蛋白、降钙素原等，但预测的特异性和敏感性有待提高[22,23]。本研究 ERCP 组和保守治疗组入院时的白细胞计数、中性粒细胞计数、C- 反应蛋白、降钙素原均显著高于对照组，淋巴细胞计数、白蛋白均显著低于对照组，且上述指标 ERCP 组和保守治疗组变化无统计学意义。说明急性胰腺炎发生时，机体的炎症反应促使大量的营养物质被消耗，导致白蛋白水平降低，机体血浆白蛋白含量的高低与危重症患者的病情和预后表现出正相关，有利于预测预后[24]。本研究显示在 ERCP 组和保守治疗组中，术后 1 d 血浆白蛋白水平低于术前 1 d，但是术后 3 d、术后 7 d 显著高于术前 1 d，且 ERCP 组术后术后 3 d、术后 7 d 血浆白蛋白水平显著高于保守治疗组。从机制上分析，手术应激可使得机体内的血浆白蛋白水水平迅速降低，不过术后在蛋白能量摄入明显增加时，血浆白蛋白即会有明显的回升[25,26]。

白蛋白的氨基酸序列及其空间结构非常保守，在机体中扮演重要的功能[27,28]。本研究显示 logistic 回归分析显示白蛋白、降钙素原为影响患者预后的主要危险因素。主要在于急性胰腺炎手术后的机体应激反应较重，伴随大量炎症因子的释放，白蛋白可从血管腔内漏出组织间隙，造成了白蛋白的稀释。积极地营养支持可加速组织的修复及调控机体的免疫功能，减少组织水肿，有利于白蛋白水平恢复正常[29,30]。不过本研究也有一定的不足，并不能对各个因素进行充分的匹配以排除其影响，且观察时间点比较短，将在后续研究中将多种因素的影响加以考虑，从而得到更加明确的结论。

总之，急性胰腺炎患者经内镜逆行胰胆管造影手术前后血浆白蛋白水平有显著波动，白蛋白、降钙素原与患者预后显著相关，可预测患者的预后。

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