

·论著·

早期胰管支架置入治疗急性胰腺炎的 临床疗效

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【摘要】 目的 探讨早期胰管支架置入治疗急性胰腺炎的临床疗效。**方法** 采用回顾性描述性研究方法。收集 2011 年 10 月至 2017 年 12 月宁夏医科大学总医院收治的 201 例急性胰腺炎病人的临床资料;男 106 例,女 95 例;中位年龄为 62 岁,年龄范围为 18~90 岁。201 例病人中,178 例为中度重症急性胰腺炎,23 例为重度重症急性胰腺炎。病人入院后 48 h 内行胰管支架置入治疗急性胰腺炎。观察指标:(1)治疗情况。(2)随访情况。采用门诊及电话方式进行随访,了解病人术后急性胰腺炎复发情况。随访时间截至 2019 年 6 月。正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较采用独立样本 t 检验,前后比较采用配对样本 t 检验;偏态分布的计量资料以 $M(P25, P75)$ 或 $M(\text{范围})$ 表示,组间比较采用 Mann-Whitney U 检验,前后比较采用 Wilcoxon 符号秩和检验。计数资料以绝对数或百分比表示,组间比较采用 χ^2 检验。**结果** (1)治疗情况:201 例病人均成功完成早期胰管支架置入,63 例术中可见白色絮状物堵塞胰管。201 例病人入院到手术等待时间为 10 h(4 h, 22 h),手术时间为 (35 ± 15) min,首次经口进食时间为 3 d(2 d, 5 d),总住院时间为 6 d(5 d, 10 d),住院费用为 3.8 万元(3.0 万元, 4.9 万元)。201 例病人中,22 例转重症监护室治疗(其中 1 例重度重症病人住院期间死亡,1 例中度重症和 7 例重度重症病人自动出院);25 例发生局部并发症,其中 17 例为胰腺感染性坏死,7 例为胰腺包裹性坏死,1 例为脾梗死,经外科干预或保守治疗后均治愈。进一步分析,178 例中度重症病人和 23 例重度重症病人转重症监护室治疗、外科干预治疗、首次经口进食时间、总住院时间、自动出院分别为 6 例、11 例、3 d(2 d, 5 d)、6 d(5 d, 10 d)、1 例和 16 例、5 例、7 d(4 d, 9 d)、9 d(7 d, 17 d)、7 例,两者上述指标比较,差异均有统计学意义($\chi^2=91.561, 6.730, Z=6.485, 5.463, \chi^2=47.561, P<0.05$)。201 例病人入院前和入院 48 h 白细胞计数、血清淀粉酶、急性生理与慢性健康评分 II 评分分别为 $(14 \pm 6) \times 10^9/L$ 、928 U/L(411 U/L, 1 588 U/L)、 (9 ± 5) 分和 $(10 \pm 4) \times 10^9/L$ 、132 U/L(72 U/L, 275 U/L)、 (6 ± 4) 分,病人入院前和入院 48 h 上述指标比较,差异均有统计学意义($t=12.219, Z=11.639, t=16.016, P<0.05$)。(2)随访情况:201 例病人中,153 例获得随访,随访时间为 40 个月(27 个月, 55 个月)。153 例病人中,32 例急性胰腺炎复发。**结论** 早期胰管支架置入治疗急性胰腺炎安全、可行。

【关键词】 胰腺炎; 急性; 胰管支架; 内镜; 内镜逆行胰胆管造影

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Clinical efficacy of early pancreatic duct stenting in the treatment of acute pancreatitis

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【Abstract】 Objective To investigate the clinical efficacy of early pancreatic duct stenting in the treatment of acute pancreatitis. **Methods** The retrospective and descriptive study was conducted. The clinical data of 201 patients with acute pancreatitis who were admitted to General Hospital of Ningxia Medical University from October 2011 to December 2017 were collected. There were 106 males and 95 females, aged from 18 to 90 years, with a median age of 62 years. Of 201 patients, there were 178 cases with moderate severe acute pancreatitis and 23 cases with serious severe acute pancreatitis. Patients were treated with pancreatic duct stenting within 48 hours after admission. Observation indicators: (1) treatment; (2) follow-up. Follow-up was conducted using outpatient examination and telephone interview to detect recurrence of acute pancreatitis after surgery up to June 2019. Measurement data with normal distribution were represented by $Mean \pm SD$, and the independent sample t test was used for comparison between groups, and the matched samples t test was used for comparison between before and after. Measurement data with skewed distribution were represented by $M(P25, P75)$ or $M(range)$, and the Mann-Whitney U test was used for comparison between groups, and the Wilcoxon signed rank sum test was used for comparison between before and after. Count data were expressed as absolute numbers or percentages, and comparison between groups was analyzed using the chi-square test. **Results** (1) Treatment: 201 patients received pancreatic duct stenting successfully, 63 of which were detected pancreatic obstruction with white-floc. The interval time from admission to surgery, operation time, time for initial oral intake, duration of hospital stay and hospital expenses of 201 patients were 10 hours (4 hours, 22 hours), (35 \pm 15) minutes, 3 days (2 days, 5 days), 6 days (5 days, 10 days) and 3.8 \times 10⁴ yuan (3.0 \times 10⁴ yuan, 4.9 \times 10⁴ yuan). Of 201 patients, 22 patients were transferred to intensive care unit, including 1 case with serious severe underwent in-hospital death and 1 case with moderate severe and 7 cases with serious severe underwent auto-discharge from hospital. There were 25 cases with local complications, including 17 cases with pancreatic infectious necrosis, 7 cases with pancreatic walled-off necrosis and 1 case with spleen infarction. All 25 patients were cured after surgical intervention or conservative treatment. Further analysis showed that cases being transferred to intensive care unit, cases undergoing surgical treatment, the time for initial oral intake, duration of hospital stay and cases undergoing auto-discharge from hospital were 6, 11, 3 days (2 days, 5 days), 6 days (5 days, 10 days) and 1 for the 178 moderate severe cases, versus 16, 5, 7 days (4 days, 9 days), 9 days (7 days, 17 days) and 7 for the 23 serious severe cases, showing significant differences ($\chi^2=91.561$, 6.730, $Z=6.485$, 5.463, $\chi^2=47.561$, $P<0.05$). The white blood cell count, serum amylase indexes and chronic health evaluation II score of 201 patients were (14 \pm 6) \times 10⁹/L, 928 U/L (411 U/L, 1 588 U/L), 9 \pm 5 before admission, versus (10 \pm 4) \times 10⁹/L, 132 U/L (72 U/L, 275 U/L), 6 \pm 4 at 48 hours after admission, respectively, showing significant differences ($t=12.219$, $Z=11.639$, $t=16.016$, $P<0.05$). (2) Follow-up: of 201 patients, 153 cases were followed up for 40 months (27 months, 55 months). During the follow-up, 32 of the 153 cases had recurrence of acute pancreatitis. **Conclusion** Early pancreatic duct stenting is safe and feasible in the treatment of acute pancreatitis.

【Key words】 Pancreatitis; Acute; Pancreatic duct stent; Endoscopy; Endoscopic retrograde cholangiopancreatography

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急性胰腺炎是消化系统常见疾病之一,重症病人常伴器官功能衰竭及局部和全身并发症,病死率高、病程长、医疗费用高,给病人带来巨大痛苦及经济负担。

急性胰腺炎病因多样,发病机制复杂,临床发现急性胰腺炎病人胰液分泌功能正常但排出不通畅,这激化了急性胰腺炎的病情。

本研究回顾性分析 2011 年 10 月至 2017 年 12 月宁夏医科大学总医院肝胆外科收治的 201 例急性胰腺炎病人的临床资料,探讨早期胰管支架置入治疗急性胰腺炎的临床疗效。

资料与方法

一、一般资料

采用回顾性描述性研究方法。收集 201 例急性胰腺炎病人的临床资料;男 106 例,女 95 例;中位年龄为 62 岁,年龄范围为 18~90 岁。201 例病人中,178 例为中度重症急性胰腺炎,23 例为重度重症急性胰腺炎;161 例为胆源性急性胰腺炎,40 例为非胆源性胰腺炎(18 例高甘油三酯血症、3 例胆道系统肿瘤、2 例胰管畸形、1 例酒精性、1 例先天性胆管扩张症、15 例特发性);有胰腺炎病史 20 例。201 例病人发病到入院时间为 2 d(1 d, 3 d),入院时 CT 检查评分为 3 分(2 分, 4 分),101 例合并单个或多个器官功能衰竭,其中 23 例重度重症病人均合并器官功能衰竭。本研究通过宁夏医科大学总医院医学伦理委员会审批,批号为 2019-466。病人及家属均签署知情同意书。

二、纳入标准和排除标准

纳入标准:(1)满足 2012 年修订版亚特兰大标准中度重症及重度重症急性胰腺炎病人诊断。(2)年龄为 18~90 岁。

排除标准:(1)妊娠期急性胰腺炎。(2)经胰管支架置入术治愈后,急性胰腺炎复发的病人。(3)慢性胰腺炎急性发作。(4)入院后>48 h 行胰管支架置入。

三、治疗方法

手术治疗:病人入院后 48 h 内行胰管支架置入治疗。病人术前禁食>12 h,术前 15 min 肌肉注射丁溴东莨菪碱 10 mg,哌替啶 75 mg。采用电子十二指肠镜(TJF240、TJF-260V、JF-260V,日本 OLYMPUS 公司产品),通过食管、胃,于十二指肠内侧十二指肠乳头插管置入导丝(ACRO-35-450,美国 COOK®公司产品),十二指肠镜透视见导丝沿胰管方向行进(图 1),沿导丝插入乳头括约肌切开刀(KD-V411M-720,日本 OLYMPUS 公司产品)进行胰管抽吸,如胰管内存在明确阻塞物阻塞胰液引流,可一并抽出,沿导丝置入胰管支架(外径 5~7 Fr,长度 4~12 cm,美国 COOK®公司产品)通畅引流。如病人合并胆道系统疾病,需同时行内镜下胆道造影及胆道取石、胆道引流,依据病情决定是否行十二

指肠乳头括约肌切开。

围手术期管理:病人合并 WBC、C-反应蛋白升高者,使用抗菌药物治疗。需要呼吸功能支持、严重器官功能衰竭或术后麻醉恢复不佳者,转 ICU 加强治疗。每天评估病人病情,恶心、腹痛腹胀症状缓解(数字评分法疼痛评分 ≤ 2 分)、血清淀粉酶下降至正常值上限 3 倍以下者恢复经口进食。无疾病及手术相关并发症、WBC 及体温正常且可完全耐受经口进食者达到出院指征。术后 1~2 个月门诊拔除胰管支架。

四、观察指标和评价标准

观察指标:(1)治疗情况包括手术情况,入院到手术等待时间,手术时间,首次经口进食时间,总住院时间,住院费用,并发症及治疗情况,WBC、血清淀粉酶及急性生理与慢性健康评分 II (acute physiology and chronic health evaluation, APACHE II) 评分情况。(2)随访情况:获得随访病人例数、随访时间、病人急性胰腺炎复发情况。

评价标准:(1)急性胰腺炎的诊断标准、分级标准、局部并发症依照 2012 年修订版亚特兰大标准^[1]。(2)CT 检查评分标准依照 Balthazar CT 分级标准进行^[2]。并由 1 名经验丰富的腹部放射科医师审查。(3)恢复经口进食时间为可耐受经口进食并进食后无腹痛、恶心等症状再次加重的时间。

五、随访

采用门诊及电话方式进行随访,了解病人术后急性胰腺炎复发情况。随访时间截至 2019 年 6 月。

六、统计学分析

应用 SPSS 22.0 统计软件进行分析。正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较采用独立样本 t 检验,前后比较采用配对样本 t 检验;偏态分布的计量资料以 $M(P25, P75)$ 或 $M(\text{范围})$ 表示,组间比较采用 Mann-Whitney U 检验,前后比较采用 Wilcoxon 符号秩和检验。计数资料以绝对数或百分比表示,组间比较采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

结 果

一、治疗情况

201 例病人均成功完成早期胰管支架置入,63 例术中可见白色絮状物堵塞胰管(图 2)。201 例病人入院到手术等待时间为 10 h(4 h, 22 h),手术时间为 (35 ± 15) min,首次经口进食时间为 3 d(2 d, 5 d),总住院时间为 6 d(5 d, 10 d),住院费用为 3.8 万元

(3.0 万元, 4.9 万元)。201 例病人中, 22 例转 ICU 治疗(其中 1 例重度重症病人住院期间死亡, 1 例中度重症和 7 例重度重症病人自动出院); 25 例发生局部并发症, 其中 17 例为胰腺感染性坏死, 7 例为胰腺包裹性坏死, 1 例为脾梗死, 经外科干预或保守治疗后均治愈。进一步分析, 178 例中度重症病人和 23 例重度重症病人转 ICU 治疗、外科干预治疗、首次经口进食时间、总住院时间、自动出院分别为 6 例、11 例、3 d(2 d, 5 d)、6 d(5 d, 10 d)、1 例和 16 例、5 例、7 d(4 d, 9 d)、9 d(7 d, 17 d)、7 例, 两者上述指标比较, 差异均有统计学意义($\chi^2=91.561, 6.730, Z=6.485, 5.463, \chi^2=47.561, P<0.05$)。

201 例病人入院前和入院 48 h WBC 计数、血清淀粉酶、APACHE II 评分分别为 $(14\pm 6)\times 10^9/L$ 、928 U/L(411 U/L, 1 588 U/L)、 (9 ± 5) 分和 $(10\pm 4)\times 10^9/L$ 、132 U/L(72 U/L, 275 U/L)、 (6 ± 4) 分, 病人入院前和入院 48 h 上述指标比较, 差异均有统计学意义($t=12.219, Z=11.639, t=16.016, P<0.05$)。

二、随访情况

201 例病人中, 153 例获得随访, 随访时间为 40 个月(27 个月, 55 个月)。153 例病人中, 32 例急性胰腺炎复发。

讨 论

重症急性胰腺炎起病急骤、病情凶险、病程长, 其发病机制尚未完全明确, 目前常以对症及并发症治疗为主。病人在疾病早期即出现全身炎症反应综合征, 甚至严重的全身重要器官功能障碍。因

此, 早期以重要脏器功能保护为主, 辅以疼痛控制、抑制消化酶分泌、营养支持、预防感染等治疗; 后期如胰腺及周围组织局部炎症未得到及时吸收, 则形成包裹性坏死、感染性坏死, 常需行穿刺或手术清理坏死组织^[3-5]。虽然医疗技术在不断革新, 但是重症急性胰腺炎的发病仍逐年递增, 病死率高^[6-7]。

胰液引流不通畅在急性胰腺炎的发病和进展过程中起重要作用。1989 年英国研究者 Harvey 等^[8]通过在猫的胰管内灌注脱氧胆酸、胃内灌注 40% 乙醇、部分夹闭胰管, 模拟胆汁反流、酒精、胰管阻塞病因, 结果显示: 动物均发展为急性胰腺炎, 胰管内压力明显升高, 且胰管对大分子物质通透性明显增加, 部分胰管阻塞动物模型胰腺实质出血坏死。该研究结果显示: 上述 3 种类型急性胰腺炎均存在胰管高压, 且胰管高压引起的胰管对大分子物质通透性增加可能是胰酶在胰腺内异常激活的原因。其后续研究结果显示: 动物急性胰腺炎严重程度越高, 其胰管内压力越高, 且壶腹部周围组织炎症水肿, 会加重胰管高压; 反之, 胰管压力增加可诱发更严重急性胰腺炎^[9-10]。胆汁反流诱发胰管阻塞和胰管高压可引起急性胰腺炎^[11]。有研究结果显示: 胰管阻塞及高压, 或由十二指肠乳头水肿、Oddi 括约肌痉挛引起的胰管阻塞及高压, 在急性胰腺炎的发病中起重要作用^[12-17]。本研究中, 63 例病人胰管内存在固态阻塞物, 影响胰液排出, 置入胰管支架通畅胰管引流后, 病人症状明显改善。因此, 对急性胰腺炎病人胰管疏通、减压治疗非常重要。

胰管支架置入最常见的内镜手术相关并发症为

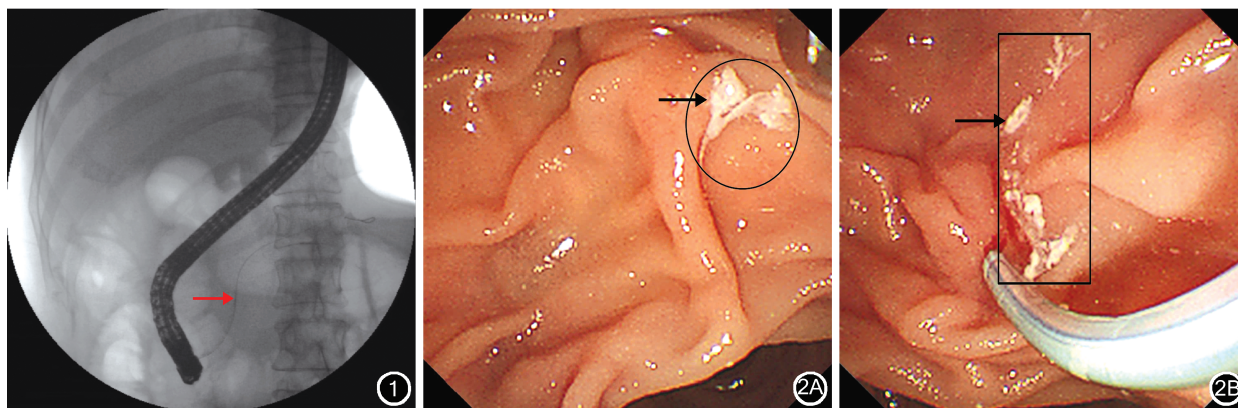


图1 十二指肠镜透视见导丝沿胰管方向走行(→) 图2 急性胰腺炎病人术中情况 2A: 内镜检查示十二指肠乳头口可见白色絮状物溢出(→); 2B: 内镜检查示胰管插管成功后十二指肠乳头口大量胰管内阻塞物持续排出(→)

Figure 1 Fluoroscopy showed indwelling guidewire running along the pancreatic duct (→) Figure 2 Intraoperative status of acute pancreatitis patients 2A: Endoscopy showed white-floc (→) at duodenal papilla ostium; 2B: Endoscopy showed excretion of obstruction (→) from pancreatic duct at duodenal papilla ostium after pancreatic duct cannulation

出血、穿孔及 ERCP 后胰腺炎 (post-ERCP pancreatitis, PEP)^[18]。胰管支架置入是预防 PEP 发生和发生 PEP 后拯救的重要措施^[19-21]。避免内镜相关并发症发生与内镜医师经验密不可分,笔者所在单位每年完成 ERCP 例数>1 700 例,本研究病人行早期胰管支架置入未增加内镜相关并发症发生风险。重症急性胰腺炎早期,全身炎症反应及器官功能衰竭是造成病人死亡的最主要原因,在持续存在器官功能衰竭病人中,病死率>30%^[22]。早期手术治疗可增加急性胰腺炎病人病死率^[23]。但内镜手术是相对微创、快捷、安全的干预手段,如对并发严重器官功能衰竭的重症急性胆管炎病人,经内镜逆行胆管造影术仍是挽救病人生命的重要措施^[24-25]。10%~20% 急性胰腺炎病人后期可合并局部并发症,其中约 1/3 病人形成感染性坏死,重度重症胰腺炎病人感染性坏死发生率>20%,坏死组织需再行外科清理及引流^[26-29]。本研究 201 例病人中,17 例发生胰腺感染性坏死。胰液引流不通畅,胰管压力增加可导致胰管通透性和胰液外溢均增加,31%~44% 坏死性胰腺炎病人合并胰管破裂,包裹性坏死合并胰管破裂>80%^[8,30-32]。有效胰管减压和引流可以减少胰液外溢,从而降低局部并发症发生率和感染率。

急性胰腺炎病人经口进食需等待胃肠道功能恢复及血清淀粉酶下降^[33]。有研究结果显示:轻症急性胰腺炎病人多数可早期耐受经口进食,但部分重症病人因经口进食诱发腹痛、呕吐等需再次禁食^[34-36]。重症病人行肠内营养支持,可防止感染性并发症发生^[36-40]。本研究中,病人经口进食需待临床症状缓解,血清淀粉酶下降至正常值上限 3 倍以下,在胰管支架置入后,经口进食时间为 3 d (2 d, 5 d)。同期研究结果显示:轻症胰腺炎病人症状缓解后恢复进食仍需 5 d^[34]。有研究结果显示:我国重症急性胰腺炎住院时间为 13~35 d,住院费用为 (3.5~6.2) 万元^[41]。而本研究病人总住院时间为 6 d (5 d, 10 d),住院费用为 3.8 万元 (3.0 万元, 4.9 万元)。急性胰腺炎的复发率较高,本研究复发率为 20.92% (32/153),与既往研究结果相似^[42]。

本研究中病人行内镜治疗后, WBC 计数、血清淀粉酶、APACHE II 评分均显著下降,说明通畅胰液引流对于急性胰腺炎病人早期炎症反应控制有效。

综上,早期胰管支架置入治疗急性胰腺炎安

全、可行。但本研究为单中心、回顾性研究,有待前瞻性临床对照试验研究进一步验证。

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参 考 文 献

- [1] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus[J]. Gut, 2013,62(1):102-111. DOI:10.1136/gutjnl-2012-302779.
- [2] Raghuwanshi S, Gupta R, Vyas MM, et al. CT Evaluation of acute pancreatitis and its prognostic correlation with CT severity index[J]. J Clin Diagn Res, 2016,10(6):TC06-11. DOI:10.7860/JCDR/2016/19849.7934.
- [3] 中华医学会消化病学分会胰腺疾病学组,中华胰腺病杂志编辑委员会,中华消化杂志编辑委员会. 中国急性胰腺炎诊治指南(2019 年,沈阳)[J]. 中华消化杂志, 2019,39(11):721-730. DOI:10.3760/cma.j.issn.0254-1432.2019.11.001.
- [4] 姚黎超,汤志刚. 急性胰腺炎的早期治疗[J]. 中国现代普通外科进展, 2019,22(11):909-911. DOI:10.3969/j.issn.1009-9905.2019.11.021.
- [5] 王春友. 急性坏死性胰腺炎的外科干预:时机比技术更重要[J]. 中华消化外科杂志, 2020,19(4):366-369. DOI:10.3760/cma.j.cn115610-20200320-00184.
- [6] Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018[J]. Gastroenterology, 2019,156(1):254-272.e11. DOI:10.1053/j.gastro.2018.08.063.
- [7] 赵彦,刘俐,吕辰艳,等. 重症胰腺炎患者预后生存情况及与其临床特征的相关性研究[J]. 解放军医药杂志, 2020,32(5):78-81,98. DOI:10.3969/j.issn.2095-140X.2020.05.019.
- [8] Harvey MH, Wedgwood KR, Austin JA, et al. Pancreatic duct pressure, duct permeability and acute pancreatitis[J]. Br J Surg, 1989,76(8):859-862. DOI:10.1002/bjs.1800760832.
- [9] Fujiwara H. Pressure measurement in pancreatic duct and biliary duct system in dogs with acute pancreatitis[J]. Kobe J Med Sci, 1991,37(2):47-55.
- [10] Shi CX, Chen JW, Carati CJ, et al. Effects of acute pancreatic duct obstruction on pancreatic perfusion: implication of acute pancreatic duct decompression[J]. Scand J Gastroenterol, 2002,37(11):1328-1333. DOI:10.1080/003655202761020623.
- [11] Arendt T, Nizze H, Mönig H, et al. Biliary pancreatic reflux-induced acute pancreatitis-myth or possibility? [J]. Eur J Gastroenterol Hepatol, 1999,11(3):329-335. DOI:10.1097/00042737-199903000-00019.
- [12] Buchwalow I, Schnekenburger J, Atiakshin D, et al. Oxidative stress and NO generation in the rat pancreatitis induced by pancreatic duct ligation[J]. Acta Histochem, 2017, 119(3):252-256. DOI:10.1016/j.acthis.2017.01.010.
- [13] Apte MV, Pirola RC, Wilson JS. Mechanisms of alcoholic pancreatitis[J]. J Gastroenterol Hepatol, 2010,25(12):1816-1826. DOI:10.1111/j.1440-1746.2010.06445.x.
- [14] Takahashi T, Miao Y, Kang F, et al. Susceptibility factors and cellular mechanisms underlying alcoholic pancreatitis [J]. Alcohol Clin Exp Res, 2020,44(4):777-789. DOI:10.11

- 11/acer.14304.
- [15] Wen L, Javed TA, Yimlamai D, et al. Transient high pressure in pancreatic ducts promotes inflammation and alters tight junctions via calcineurin signaling in mice[J]. *Gastroenterology*, 2018, 155(4):1250-1263.e5. DOI:10.1053/j.gastro.2018.06.036.
 - [16] Romac JM, Shahid RA, Swain SM, et al. Piezol is a mechanically activated ion channel and mediates pressure induced pancreatitis[J]. *Nat Commun*, 2018, 9(1):1715. DOI: 10.1038/s41467-018-04194-9.
 - [17] 李静,徐宁.急性重症胰腺炎七例误诊原因分析[J]. *临床误诊误治*, 2019, 32(7):1-4. DOI:10.3969/j.issn.1002-3429.2019.07.001.
 - [18] Lee HJ, Cho CM, Heo J, et al. Impact of hospital volume and the experience of endoscopist on adverse events related to endoscopic retrograde cholangiopancreatography: a prospective observational study[J]. *Gut Liver*, 2020, 14(2): 257-264. DOI:10.5009/gnl18537.
 - [19] Smeets X, Bouhouch N, Buxbaum J, et al. The revised Atlanta criteria more accurately reflect severity of post-ERCP pancreatitis compared to the consensus criteria[J]. *United European Gastroenterol J*, 2019, 7(4):557-564. DOI: 10.1177/2050640619834839.
 - [20] Fan JH, Qian JB, Wang YM, et al. Updated meta-analysis of pancreatic stent placement in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis [J]. *World J Gastroenterol*, 2015, 21(24):7577-7583. DOI: 10.3748/wjg.v21.i24.7577.
 - [21] Kerdsirichairat T, Attam R, Arain M, et al. Urgent ERCP with pancreatic stent placement or replacement for salvage of post-ERCP pancreatitis[J]. *Endoscopy*, 2014, 46(12):1085-1094. DOI:10.1055/s-0034-1377750.
 - [22] De Rai P, Zerbi A, Castoldi L, et al. Surgical management of acute pancreatitis in Italy: lessons from a prospective multicentre study[J]. *HPB (Oxford)*, 2010, 12(9):597-604. DOI:10.1111/j.1477-2574.2010.00201.x.
 - [23] Zhang H, Gao L, Mao WJ, et al. Early versus delayed intervention in necrotizing acute pancreatitis complicated by persistent organ failure[J]. *Hepatobiliary Pancreat Dis Int*, 2021[Online ahead of print]. DOI:10.1016/j.hbpd.2020.12.019.
 - [24] Tsuchiya T, Sofuni A, Tsuji S, et al. Endoscopic management of acute cholangitis according to the TG13[J]. *Dig Endosc*, 2017, 29(Suppl 2):94-99. DOI:10.1111/den.12799.
 - [25] Iqbal U, Khara HS, Hu Y, et al. Emergent versus urgent ERCP in acute cholangitis: a systematic review and meta-analysis[J]. *Gastrointest Endosc*, 2020, 91(4): 753-760.e4. DOI:10.1016/j.gie.2019.09.040.
 - [26] van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotizing pancreatitis: a multicentre randomised trial [J]. *Lancet*, 2018, 391(10115):51-58. DOI:10.1016/S0140-6736(17)32404-2.
 - [27] Hollemans RA, Bakker OJ, Boermeester MA, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis [J]. *Gastroenterology*, 2019, 156(4):1016-1026. DOI:10.1053/j.gastro.2018.10.045.
 - [28] 孙备,李冠群.重症急性胰腺炎局部并发症外科干预策略[J]. *中华消化外科杂志*, 2020, 19(4):379-383. DOI:10.3760/cma.j.cn115610-20200121-00040.
 - [29] Karjula H, Nordblad Schmidt P, Mäkelä J, et al. Prophylactic pancreatic duct stenting in severe acute necrotizing pancreatitis: a prospective randomized study[J]. *Endoscopy*, 2019, 51(11):1027-1034. DOI:10.1055/a-0865-1960.
 - [30] Lau ST, Simchuk EJ, Kozarek RA, et al. A pancreatic ductal leak should be sought to direct treatment in patients with acute pancreatitis[J]. *Am J Surg*, 2001, 181(5):411-415. DOI: 10.1016/s0002-9610(01)00606-7.
 - [31] Uomo G, Molino D, Visconti M, et al. The incidence of main pancreatic duct disruption in severe biliary pancreatitis [J]. *Am J Surg*, 1998, 176(1):49-52. DOI:10.1016/s0002-9610(98)00097-x.
 - [32] Jagielski M, Smoczyński M, Adrych K. The role of endoscopic treatment of pancreatic duct disruption in patients with walled-off pancreatic necrosis[J]. *Surg Endosc*, 2018, 32(12):4939-4952. DOI:10.1007/s00464-018-6255-4.
 - [33] Chebli JM, Gaburri PD, De Souza AF, et al. Oral refeeding in patients with mild acute pancreatitis: prevalence and risk factors of relapsing abdominal pain[J]. *J Gastroenterol Hepatol*, 2005, 20(9):1385-1389. DOI:10.1111/j.1440-1746.2005.03986.x.
 - [34] Dong E, Chang JI, Verma D, et al. Enhanced recovery in mild acute pancreatitis: a randomized controlled trial[J]. *Pancreas*, 2019, 48(2):176-181. DOI:10.1097/MPA.0000000000001225.
 - [35] Bakker OJ, van Brunschot S, van Santvoort HC, et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis[J]. *N Engl J Med*, 2014, 371(21):1983-1993. DOI: 10.1056/NEJMoa1404393.
 - [36] Al-Omran M, Albalawi ZH, Tashkandi MF, et al. Enteral versus parenteral nutrition for acute pancreatitis[J]. *Cochrane Database Syst Rev*, 2010, 2010(1):CD002837. DOI:10.1002/14651858.CD002837.pub2.
 - [37] 余婷媛,税金凤,李亚男.奥美拉唑联合免疫肠内营养治疗重症急性胰腺炎的临床疗效及对T淋巴细胞亚群和细胞因子的影响[J]. *解放军医药杂志*, 2018, 30(3):73-76. DOI: 10.3969/j.issn.2095-140X.2018.03.019.
 - [38] 赵红,肖静蓉,于海燕.生长抑素联合白蛋白治疗急性胰腺炎患者的效果及对胰腺功能和免疫功能的影响[J]. *临床误诊误治*, 2021, 34(1):26-30. DOI:10.3969/j.issn.1002-3429.2021.01.007.
 - [39] 李军,李静喆.早期肠内营养联合腹腔引流对重症急性胰腺炎患者免疫功能及营养状态的影响[J]. *中国现代普通外科进展*, 2020, 23(2):147-149. DOI:10.3969/j.issn.1009-9905.2020.02.018.
 - [40] 中华医学会急诊分会,京津冀急诊急救联盟,北京医学会急诊分会,等.急性胰腺炎急诊诊断及治疗专家共识[J]. *临床肝胆病杂志*, 2021, 37(5):1034-1041. DOI:10.3969/j.issn.1001-5256.2021.05.012.
 - [41] 李勇,卢绮萍,刘升辉.谷氨酰胺强化营养支持治疗重症急性胰腺炎疗效的Meta分析[J]. *中华消化外科杂志*, 2014, 13(7):525-530. DOI:10.3760/cma.j.issn.1673-9752.2014.07.007.
 - [42] Magnusdottir BA, Baldursdottir MB, Kalaitzakis E, et al. Risk factors for chronic and recurrent pancreatitis after first attack of acute pancreatitis[J]. *Scand J Gastroenterol*, 2019, 54(1):87-94. DOI:10.1080/00365521.2018.1550670.