

急性胰腺炎液体复苏治疗现状

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摘要

急性胰腺炎已经成为胃肠道疾病入院最常见的疾病之一, 因其发病快, 并可以导致严重的并发症和死亡率且住院时间长和花费高。急性胰腺炎是一种复杂的疾病, 其病程多变, 往往难以在其发展的早期预测。大约80%的患者发展为轻度严重的严重疾病(48小时内无器官衰竭)。胰腺炎是胰腺内炎症过程的结果, 通常会伴随腹痛、恶心和呕吐等非特异性症状。大多数患者不会发生严重的并发症, 但有一小部分病例导致显著的发病率和死亡率。而对于紧急就诊的急性胰腺炎的病人, 评估通常包括实验室和超声评估, 而对于早期急性胰腺炎的病人, 针对病人的个体化治疗进行液体复苏是必要的。然而, 五分之一的患者发展为严重疾病, 死亡率约为20%。急性胰腺炎是一种常见的和异质性的疾病, 具有显著的发病率。急性胰腺炎管理的最佳实践集中在分诊、水合作用和肠内喂养。

关键词

急性胰腺炎, 液体复苏, 液体平衡

Current Status of Fluid Resuscitation Therapy for Acute Pancreatitis

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Abstract

Acute pancreatitis has become one of the most common hospital admissions for gastrointestinal

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disorders because of its rapid onset, which can lead to serious complications and mortality with long and costly hospital stays. Acute pancreatitis is a complex disease with a variable course that is often difficult to predict early in its development. Approximately 80% of patients develop severe disease of mild severity (no organ failure within 48 hours). Pancreatitis is the result of an inflammatory process within the pancreas and is usually accompanied by non-specific symptoms such as abdominal pain, nausea and vomiting. Most patients do not develop serious complications, but a small percentage of cases result in significant morbidity and mortality. Whereas in patients presenting urgently with acute pancreatitis, the evaluation usually includes laboratory and ultrasound assessment; in patients with early acute pancreatitis, fluid resuscitation is necessary to individualize the patient's treatment. However, one in five patients develop severe disease with a mortality rate of approximately 20%. Acute pancreatitis is a common and heterogeneous disease with significant morbidity. Best practices in the management of acute pancreatitis focus on triage, hydration, and enteral feeding.

Keywords

Acute Pancreatitis, Fluid Resuscitation, Fluid Balance

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1. 病理及生理

胰腺炎是一种胰腺炎性疾病，其中以胰腺组织自消化为特点。细胞损伤最初发生，导致胰蛋白酶原的激活和巨噬细胞和中性粒细胞的聚集。胰蛋白酶原对胰蛋白酶的激活会导致进一步的细胞损伤，以及其他消化酶的激活，最终导致胰腺组织的大量破坏。在大多数发展为急性胰腺炎的个体中，这种正反馈回路会自动停止。然而，在一些特定的患者中，疾病进展并导致更严重的全身性疾病，导致弥漫性胰腺坏死和潜在的感染[1] [2]。

急性胰腺炎的病理生理学包括腺泡细胞炎症的复杂级联事件、免疫系统的参与和全身病理结果[3]。腺泡内消化酶原的过早激活是 AP 的早期标志之一。由此产生的胰腺的自动消化导致促炎介质的释放，如肿瘤坏死因子- α 、白细胞介素(IL)-1 β 、IL-6，这些介质与微循环混合，导致血管通透性增加、水肿、出血和胰腺坏死[4] [5] [6]。严重的腺泡细胞损伤和放大的炎症反应会导致全身性炎症反应综合征(SIRS)和多器官功能障碍综合征(MODS)，最终导致 AP 相关的死亡率[7] [8] [9]。免疫系统被认为在 AP 疾病的发病机制中起着重要的作用。复杂的免疫事件是 AP 进展的基础。

这些患者由于炎症反应严重，大量血管内液体渗漏、腹膜后腔、肺实质等疏松软组织间质内液体滞留，加上呕吐和禁食，导致有效循环血量不足，甚至出现低血容量性休克。此外，有效循环血量不足容易引起 MODS，甚至导致死亡。积极有效的液体复苏应迅速恢复血流动力学参数，消除氧债，使动脉血乳酸恢复到正常范围[10] [11]。

急性胰腺炎潜在的病因是胰管阻塞增加胰腺管压力，导致回流到胰腺，激活胰腺内的胰蛋白酶原，导致随后的细胞损伤[12]。其他引起机械性梗阻的原因(如胰腺癌、Oddi 功能障碍的括约肌、内镜后逆行胰胆管造影[ERCP])可能也有类似的病因。ERCP 后胰腺炎的危险因素包括 Oddi 功能障碍 rtyiop 括约肌史、女性、年龄以及反复尝试插管等[13]。

2. 液体复苏

液体复苏是急性胰腺炎的主要治疗方法。患者通常出现在多次恶心和呕吐发作后,并出现容量不足。炎症介质的释放也增加血管通透性和进入第三间隙[14]。因此认为住院护理 24 小时后的液体复苏不足与胰腺坏死率的增加有关[15]。故对这些患者经常进行大容量的液体复苏。目前国内外早期液体复苏均推荐“目标导向治疗”的策略,液体复苏评估的指标包括心率、平均动脉压、尿量、血尿素氮(blood urea nitrogen, BUN)、红细胞压积(hematocrit, HCT)、中心静脉压、脉搏指数连续心排出量监测等[16] [17] [18]。然而应该承认,支持这些建议的证据相对较弱,与非靶向性治疗相比,没有明确的证据表明,定向治疗导致显著改善重要的结果,如死亡率、预防胰腺坏死,或减少持续多器官衰竭的速度[19]。使用生理指标来指导初始液体复苏对于确保足够的器官灌注和避免过度积极的液体治疗都很重要,这可能与急性胰腺炎的危害相关,包括呼吸并发症和腹腔室综合征[1] [20]。需要注意的是,积极的液体复苏在入院的前 12~24 小时最有用,在此之后一般应减少液体超载[21] [22] [23]。

在一些动物模型中我们发现,胰腺的低灌注与胰腺的坏死呈正相关性,并可进一步通过液体灌注进行纠正[24] [25] [26] [27]。有实验研究表明,胰腺微循环的损害是坏死性胰腺炎发展的主要因素[28]。因此,早期的高灌注可以防止并发症的发展。而在最近的一些随机对照试验中发现,早期的高灌注并没有明显改善患者胰腺坏死的发展[20] [29] [30]。

3. 讨论

静脉输液复苏的基本原理是提供血流动力学支持,并扩大严重耗尽的血管内空间,以帮助重要器官的灌注。不幸的是,目前还没有批准的药物来帮助抵消 AP 全身炎症引起的毛细血管渗漏。多项回顾性研究快速血液稀释,数据显示,快速体外受精治疗和使用红细胞压积和尿素氮作为标志物实现快速血液稀释是有效的[31] [32] [33] [34]。总之大多数患者(91%)患有轻度急性胰腺炎的急性胰腺炎队列中,持续性器官衰竭没有额外改善,更积极的液体复苏没有增加患者的治愈率,但是液体复苏可改善器官衰竭。因此,目前的证据支持目标液体复苏和早期口服喂养对急性胰腺炎患者是有好处的。

参考文献

- [1] Zerem, E. (2014) Treatment of Severe Acute Pancreatitis and Its Complications. *World Journal of Gastroenterology*, **20**, 13879-13892. <https://doi.org/10.3748/wjg.v20.i38.13879>
- [2] Sah, R.P., Dawra, R.K. and Saluja, A.K. (2013) New Insights into the Pathogenesis of Pancreatitis. *Current Opinion in Gastroenterology*, **29**, 523-530. <https://doi.org/10.1097/MOG.0b013e328363e399>
- [3] Shamoony, M., Deng, Y., Chen, Y.Q., et al. (2016) Therapeutic Implications of Innate Immune System in Acute Pancreatitis. *Expert Opinion on Therapeutic Targets*, **20**, 73-87. <https://doi.org/10.1517/14728222.2015.1077227>
- [4] Ramnath, R.D., Sun, J. and Bhatia, M. (2010) PKC Delta Mediates Pro-Inflammatory Responses in a Mouse Model of Caerulein-Induced Acute Pancreatitis. *Journal of Molecular Medicine*, **88**, 1055-1063. <https://doi.org/10.1007/s00109-010-0647-9>
- [5] Bhatia, M., Neoptolemos, J.P. and Slavin, J. (2001) Inflammatory Mediators as Therapeutic Targets in Acute Pancreatitis. *Current Opinion in Investigational Drugs*, **2**, 496-501. [https://doi.org/10.1002/\(SICI\)1096-9896\(200002\)190:2<117::AID-PATH494>3.0.CO;2-K](https://doi.org/10.1002/(SICI)1096-9896(200002)190:2<117::AID-PATH494>3.0.CO;2-K)
- [6] Bhatia, M. (2002) Novel Therapeutic Targets for Acute Pancreatitis and Associated Multiple Organ Dysfunction Syndrome. *Current Drug Targets—Inflammation & Allergy*, **1**, 343-351. <https://doi.org/10.2174/1568010023344517>
- [7] Bhatia, M. (2009) Acute Pancreatitis as a Model of SIRS. *Frontiers in Bioscience*, **14**, 2042-2050. <https://doi.org/10.2741/3362>
- [8] McKay, C.J. and Buter, A. (2003) Natural History of Organ Failure in Acute Pancreatitis. *Pancreatology*, **3**, 111-114. <https://doi.org/10.1159/000070078>
- [9] Raraty, M.G., Connor, S., Criddle, D.N., et al. (2004) Acute Pancreatitis and Organ Failure: Pathophysiology, Natural

History, and Management Strategies. *Current Gastroenterology Reports*, **6**, 99-103.

<https://doi.org/10.1007/s11894-004-0035-0>

- [10] 刘大为, 邱海波, 徐媛, 等. 实用重症医学[M]. 第2版. 北京: 人民卫生出版社, 2017: 4.
- [11] 毛恩强, 李梦娇. 重症急性胰腺炎早期液体复苏与器官功能维护[J]. 中华消化杂志, 2020, 40(7): 441-443.
- [12] Wang, G.J., Gao, C.F., Wei, D., *et al.* (2009) Acute Pancreatitis: Etiology and Common Pathogenesis. *World Journal of Gastroenterology*, **15**, 1427-1430. <https://doi.org/10.3748/wjg.15.1427>
- [13] Cheng, C.L., Sherman, S., Watkins, J.L., *et al.* (2006) Risk Factors for Post-ERCP Pancreatitis: A Prospective Multi-center Study. *American Journal of Gastroenterology*, **101**, 139-147. <https://doi.org/10.1111/j.1572-0241.2006.00380.x>
- [14] Pandol, S.J., Saluja, A.K., Imrie, C.W. and Banks, P.A. (2007) Acute Pancreatitis: Bench to the Bedside. *Gastroenterology*, **132**, 1127-1151. <https://doi.org/10.1053/j.gastro.2007.01.055>
- [15] Brown, A., Baillargeon, J.D., Hughes, M.D. and Banks, P.A. (2002) Can Fluid Resuscitation Prevent Pancreatic Necrosis in Severe Acute Pancreatitis? *Pancreatology*, **2**, 104-107. <https://doi.org/10.1159/000055899>
- [16] James, T.W. and Crockett, S.D. (2018) Management of Acute Pancreatitis in the First 72 Hours. *Current Opinion in Gastroenterology*, **34**, 330-335. <https://doi.org/10.1097/MOG.0000000000000456>
- [17] 杜奕奇, 陈其奎, 李宏宇, 等. 中国急性胰腺炎诊治指南(2019年, 沈阳) [J]. 临床肝胆病杂志, 2019, 35(12): 2706-2711.
- [18] Sun, Y., Lu, Z.H., Zhang, X.S., *et al.* (2015) The Effects of Fluid Resuscitation According to PiCCO on the Early Stage of Severe Acute Pancreatitis. *Pancreatology*, **15**, 497-502. <https://doi.org/10.1016/j.pan.2015.06.006>
- [19] Crockett, S.D., Wani, S., Gardner, T.B., *et al.* (2018) American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*, **154**, 1096-1101. <https://doi.org/10.1053/j.gastro.2018.01.032>
- [20] De-Madaria, E., Soler-Sala, G., Sanchez-Payà, J., *et al.* (2011) Influence of Fluid Therapy on the Prognosis of Acute Pancreatitis: A Prospective Cohort Study. *American Journal of Gastroenterology*, **106**, 1843-1850. <https://doi.org/10.1038/ajg.2011.236>
- [21] Tenner, S., Baillie, J., DeWitt, J. and Vege, S.S. (2013) American College of Gastroenterology Guideline: Management of Acute Pancreatitis. *American Journal of Gastroenterology*, **108**, 1400. <https://doi.org/10.1038/ajg.2013.218>
- [22] Gardner, T.B., Vege, S.S., Chari, S.T., *et al.* (2009) Faster Rate of Initial Fluid Resuscitation in Severe Acute Pancreatitis Diminishes In-Hospital Mortality. *Pancreatology*, **9**, 770-776. <https://doi.org/10.1159/000210022>
- [23] Warndorf, M.G., Kurtzman, J.T., Bartel, M.J., *et al.* (2011) Early Fluid Resuscitation Reduces Morbidity among Patients with Acute Pancreatitis. *Clinical Gastroenterology and Hepatology*, **9**, 705-709. <https://doi.org/10.1016/j.cgh.2011.03.032>
- [24] Kinnala, P.J., Kuttala, K.T., Grönroos, J.M., *et al.* (2002) Splanchnic and Pancreatic Tissue Perfusion in Experimental Acute Pancreatitis. *Scandinavian Journal of Gastroenterology*, **37**, 845-849. <https://doi.org/10.1080/gas.37.7.845.849>
- [25] Kusterer, K., Enghofer, M., Zendler, S., *et al.* (1991) Microcirculatory Changes in Sodium Taurocholate-Induced Pancreatitis in Rats. *American Journal of Physiology*, **260**, G346-G351. <https://doi.org/10.1152/ajpgi.1991.260.2.G346>
- [26] Juvonen, P.O., Tenhunen, J.J., Heino, A.A., *et al.* (1999) Splanchnic Tissue Perfusion in Acute Experimental Pancreatitis. *Scandinavian Journal of Gastroenterology*, **34**, 308-314. <https://doi.org/10.1080/00365529950173744>
- [27] Niederau, C., Crass, R.A., Silver, G., *et al.* (1988) Therapeutic Regimens in Acute Experimental Hemorrhagic Pancreatitis. Effects of Hydration, Oxygenation, Peritoneal Lavage, and a Potent Protease Inhibitor. *Gastroenterology*, **95**, 1648-1657. [https://doi.org/10.1016/S0016-5085\(88\)80091-X](https://doi.org/10.1016/S0016-5085(88)80091-X)
- [28] Gardner, T.B., Vege, S.S., Pearson, R.K. and Chari, S.T. (2008) Fluid Resuscitation in Acute Pancreatitis. *Clinical Gastroenterology and Hepatology*, **6**, 1070-1076. <https://doi.org/10.1016/j.cgh.2008.05.005>
- [29] Vege, S.S., DiMaggio, M.J., Forsmark, C.E., *et al.* (2018) Initial Medical Treatment of Acute Pancreatitis: American Gastroenterological Association Institute Technical Review. *Gastroenterology*, **154**, 1103-1139. <https://doi.org/10.1053/j.gastro.2018.01.031>
- [30] de-Madaria, E., Buxbaum, J.L., Maisonneuve, P., *et al.* (2022) ERICA Consortium. Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis. *The New England Journal of Medicine*, **387**, 989-1000. <https://doi.org/10.1056/NEJMoa2202884>
- [31] Buxbaum, J.L., Quezada, M., Da, B., *et al.* (2017) Early Aggressive Hydration Hastens Clinical Improvement in Mild Acute Pancreatitis. *American Journal of Gastroenterology*, **112**, 797-803. <https://doi.org/10.1038/ajg.2017.40>
- [32] Koutroumpakis, E., Wu, B.U., Bakker, O.J., *et al.* (2015) Admission Hematocrit and Rise in Blood Urea Nitrogen at 24 h Outperform Other Laboratory Markers in Predicting Persistent Organ Failure and Pancreatic Necrosis in Acute

- Pancreatitis: A Post Hoc Analysis of Three Large Prospective Databases. *American Journal of Gastroenterology*, **110**, 1707-1716. <https://doi.org/10.1038/ajg.2015.370>
- [33] Lin, S., Hong, W., Basharat, Z., *et al.* (2017) Blood Urea Nitrogen as a Predictor of Severe Acute Pancreatitis Based on the Revised Atlanta Criteriar Timing of Measurement and Cutoff Points. *Canadian Journal of Gastroenterology and Hepatology*, **2017**, Article ID: 9592831. <https://doi.org/10.1155/2017/9592831>
- [34] Valverde-Lopez, F., Matas-Cobos, A.M., Alegria-Motte, C., *et al.* (2017) BISAP, RANSON, Lactate and Others Biomarkers in Prediction of Severe Acute Pancreatitis in a European Cohort. *Journal of Gastroenterology and Hepatology*, **32**, 1649-1656. <https://doi.org/10.1111/jgh.13763>