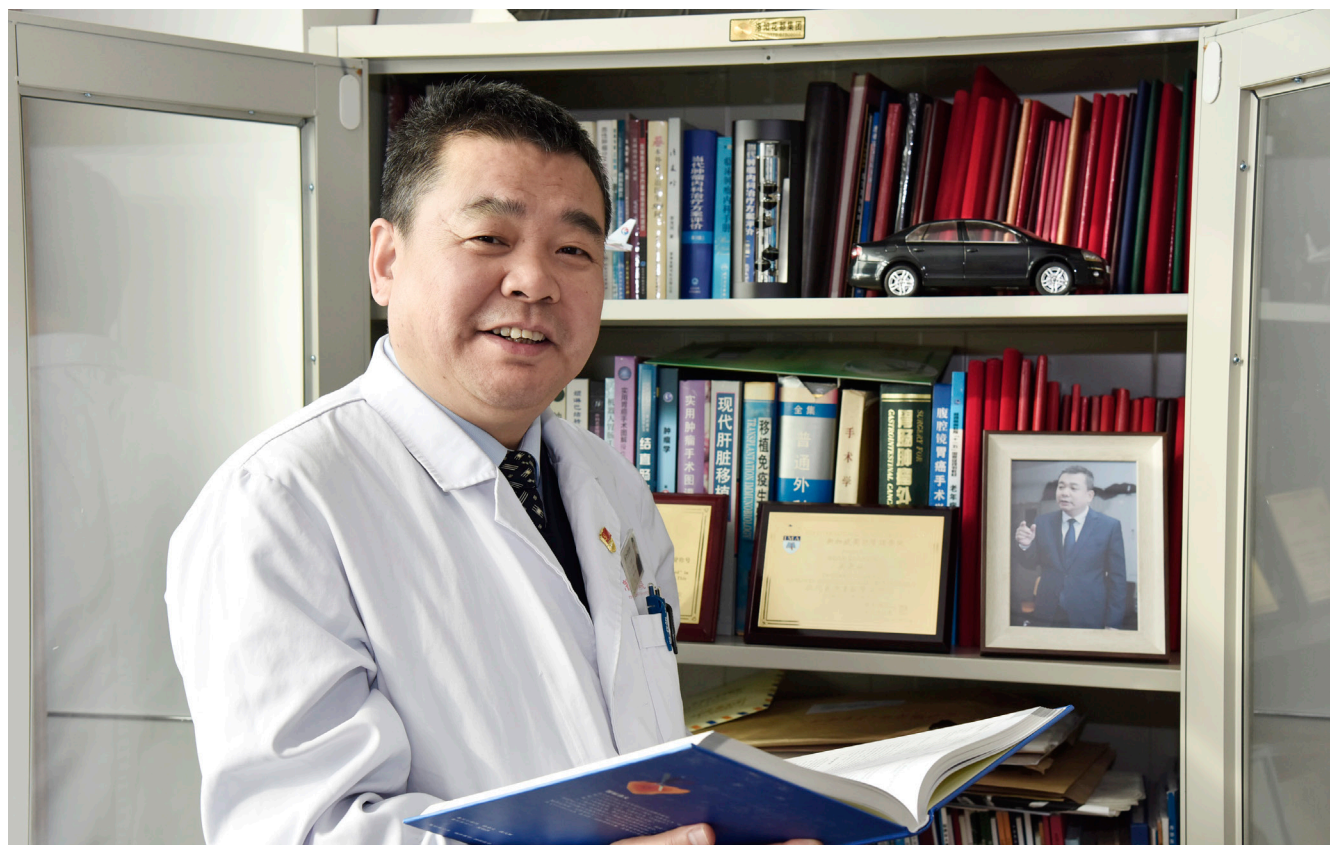


世界华人消化杂志®

WORLD CHINESE JOURNAL OF DIGESTOLOGY

Shijie Huaren Xiaohua Zazhi

2021年12月8日 第29卷 第23期 (Volume 29 Number 23)



23 / 2021

《世界华人消化杂志》是一本高质量的同行评议、开放获取和在线出版的学术刊物。本刊被国际检索系统《化学文摘(Chemical Abstracts, CA)》、《医学文摘库/医学文摘(EMBASE/Excerpta Medica, EM)》、《文摘杂志(Abstract Journal, AJ)》、Scopus、中国知网《中国期刊全文数据库(CNKI)》、《中文科技期刊数据库(CSTJ)》和《超星期刊域出版平台(Superstar Journals Database)》数据库收录。

ISSN 1009-3079



9 771009 307056

目 次

2021年12月8日 第29卷 第23期 (总第691期)

述评

- 1323 糖尿病与结直肠癌相关性的研究进展
余冠华, 姜争

基础研究

- 1334 柚皮素对酒精性肝病模型大鼠的肝保护作用
喻秀峰, 周增丽, 卢旭东, 龙思琴

临床研究

- 1341 胰管支撑管内外引流对胰十二指肠术后胰瘘影响的Meta分析
贺宸宸, 吴明东, 王春晖

文献综述

- 1349 急性胰腺炎局部并发症微创治疗的研究进展
张营, 袁二燕, 彭氏, 丁少雪, 王志强
- 1355 肠道菌群与脂肪性肝病研究新进展
李莹, 侯俊杰, 王欣, 苏帅, 王玉明, 张洁
- 1362 Paneth cell与肠道健康
韩怡敏, 高晗, 华嵘暄, 梁宸, 郭玥昕, 尚宏伟, 路欣, 徐敬东
- 1373 m6A修饰在结直肠肿瘤发生发展中的研究进展及潜在治疗价值
刘婧依, 李冰, 徐恩盼, 钟芸诗

临床实践

- 1382 基于叙事疗法的心理护理在早期胃癌根治术患者中的应用分析
姜小黎, 胡艳艳

目次

- 消 息**
- 1348 《腹痛的诊断、鉴别诊断与治疗》书讯
1354 《世界华人消化杂志》正文要求
1361 《世界华人消化杂志》修回稿须知
1372 《世界华人消化杂志》性质、刊登内容及目标

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编务 张砚梁; 送审编辑 张砚梁; 组版编辑 张砚梁; 英文编辑 王天奇;
形式规范审核编辑部主任 李香; 最终清样审核总编辑 马连生

世界华人消化杂志

Shijie Huaren Xiaohua Zazhi

吴阶平 题写封面刊名

陈可冀 题写版权刊名

(半月刊)

创刊 1993-01-15

改刊 1998-01-25

出版 2021-12-08

原刊名 新消化病学杂志

期刊名称

世界华人消化杂志

国际标准连续出版物号

ISSN 1009-3079 (print) ISSN 2219-2859 (online)

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CA 94566, USA

Telephone: +1-925-3991568

E-mail: wjcd@wjgnet.com

<http://www.wjgnet.com>

出版

百世登出版集团有限公司

Baishideng Publishing Group Inc

7041 Koll Center Parkway, Suite 160, Pleasanton,

CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

<https://www.wjgnet.com>

制作

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100025, 北京市朝阳区东四环中路
62号, 远洋国际中心D座903室
电话: +86-10-85381892

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《世界华人消化杂志》正式开通了在线办公系统(<https://www.baishideng.com>), 所有办公流程一律可以在线进行, 包括投稿、审稿、编辑、审读, 以及作者、读者和编者之间的信息反馈交流.

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定价

每期136.00元 全年24期3264.00元

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Contents

Volume 29 Number 23 December 8, 2021

EDITORIAL

- 1323 Progress in understanding relationship between diabetes and colorectal cancer
Yu GH, Jiang Z

BASIC RESEARCH

- 1334 Hepatoprotective effect of naringenin in rats with alcoholic liver disease
Yu XF, Zhou ZL, Lu XD, Long SQ

CLINICAL RESEARCH

- 1341 Impact of internal and external drainage of the pancreatic duct on pancreatic fistula after pancreaticoduodenectomy: A meta-analysis
He CC, Wu MD, Wang CC

REVIEW

- 1349 Progress in research of minimally invasive therapy of local complications of acute pancreatitis
Zhang Y, Yuan EY, Peng M, Ding SX, Wang ZQ
- 1355 New progress in research of intestinal microbiota in fatty liver disease
Li Y, Hou JJ, Wang X, Su S, Wang YM, Zhang J
- 1362 Paneth cells and intestinal health
Han YM, Gao H, Hua RX, Liang C, Guo YX, Shang HW, Lu X, Xu JD
- 1373 Research development and potential therapeutic value of m6A modification in occurrence and progression of colorectal tumors
Liu JY, Li B, Xu EQ, Zhong YS

CLINICAL PRACTICE

- 1382 Application of psychological nursing based on narrative therapy in patients with early gastric cancer undergoing radical operation
Jiang XL, Hu YY

COVER

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Indexed/Abstracted by

Chemical Abstracts, EMBASE/Excerpta Medica, Abstract Journals, Scopus, CNKI, CSTJ and Superstar Journals Database.

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Shijie Huaren Xiaohua Zazhi

Founded on January 15, 1993
Renamed on January 25, 1998
Publication date December 8, 2021

NAME OF JOURNAL
World Chinese Journal of Digestology

ISSN
 ISSN 1009-3079 (print) ISSN 2219-2859 (online)

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 Telephone: +1-925-3991568
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<https://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
 Telephone: +1-925-3991568
 E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

PRODUCTION CENTER
 Beijing Baishideng BioMed Scientific Co., Limited Room 903, Building D, Ocean International Center, No. 62 Dongsihuan Zhonglu, Chaoyang District, Beijing 100025, China
 Telephone: +86-10-85381892

PRINT SUBSCRIPTION
 RMB 136 Yuan for each issue
 RMB 3264 Yuan for one year

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 Full instructions are available online at <https://www.wjgnet.com/1009-3079/Nav/36>. If you do not have web access, please contact the editorial office.

急性胰腺炎局部并发症微创治疗的研究进展

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基金项目: 天津市教委科研计划项目, No. 2019KJ199.

作者贡献分布: 本文由张营、袁二燕进行文献检索; 张营、彭民撰写; 王志强、丁少雪审核、校对完成。

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收稿日期: 2021-08-11

修回日期: 2021-08-31

接受日期: 2021-10-08

在线出版日期: 2021-12-08

Progress in research of minimally invasive therapy of local complications of acute pancreatitis

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Supported by: Scientific Research Project of Tianjin Education Commission, No. 2019KJ199.

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Received: 2021-08-11

Revised: 2021-08-31

Accepted: 2021-10-08

Published online: 2021-12-08

Abstract

Acute pancreatitis is an inflammatory disease of the pancreas that can be life-threatening. Patients with severe acute pancreatitis require further rescue treatment in the intensive care unit. In recent years, treatment of local complications of acute pancreatitis has undergone considerable changes, including multidisciplinary team mode and individualized treatment scheme, and traditional open surgery has been gradually replaced by minimally invasive treatment. This article summarizes the progress in research on minimally invasive therapy of the local complications of acute pancreatitis in recent years.

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Key Words: Acute pancreatitis; Local complications; Minimal invasive therapy

Citation: Zhang Y, Yuan EY, Peng M, Ding SX, Wang ZQ. Progress in research of minimally invasive therapy of local complications of acute pancreatitis. *Shijie Huaren Xiaohua Zazhi* 2021; 29(23): 1349-1354

URL: <https://www.wjgnet.com/1009-3079/full/v29/i23/1349.htm>

DOI: <https://dx.doi.org/10.11569/wcjd.v29.i23.1349>

摘要

急性胰腺炎(acute pancreatitis, AP)是一种可危及生命的胰腺炎性疾病,重症急性胰腺炎患者需入重症监护病房进一步抢救治疗。近年来,其局部并发症治疗发生了相当大的变化,包括多学科综合救治模式,个体化治疗方案,传统开放性手术已逐步被微创治疗所取代。本文主要针对近几年急性胰腺炎局部并发症微创治疗相关研究进展进行综述。

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关键词: 急性胰腺炎; 局部并发症; 微创治疗

核心提要: 急性胰腺炎(acute pancreatitis, AP)治疗近几年已发生显著改变, 尤其是传统开放性手术已逐步被微创治疗所取代, 本文主要针对其局部并发症微创治疗相关研究进展进行综述, 以期对临床实际工作提供参考与理论支持。

文献来源: 张莹, 袁二燕, 彭民, 丁少雪, 王志强. 急性胰腺炎局部并发症微创治疗的研究进展. 世界华人消化杂志 2021; 29(23): 1349-1354

URL: <https://www.wjgnet.com/1009-3079/full/v29/i23/1349.htm>

DOI: <https://dx.doi.org/10.11569/wjcd.v29.i23.1349>

0 引言

急性胰腺炎(acute pancreatitis, AP)是一种常见的, 可危及患者生命的胰腺炎性疾病, 组织学特征表现为胰腺腺泡细胞破坏. 该病具有局部及全身炎症反应特点, 拥有不同的临床过程. 大多数病人表现为轻度急性胰腺炎, 这是自限性过程, 多在病程1周内自行恢复^[1], 大约20%病人发展成中度或重症急性胰腺炎, 可伴有胰周组织坏死, 甚至发展成器官功能衰竭, 目前认为重症急性胰腺炎(severe acute pancreatitis, SAP)可早期出现多器官功能衰竭, 后期出现胰腺及胰周组织坏死, 且可合并感染、消化道瘘、血管并发症等, 一般有2个死亡高峰, 死亡率大约在30%^[2]. AP患者如果出现器官功能衰竭超过48 h, 病情危重, 需收入重症监护室(intensive care unit, ICU)进一步抢救治疗^[3]. 在过去十年里, AP治疗发生了相当大的变化, 包括多学科综合救治模式, 个体化治疗方案. 由于传统手术创伤大, 术后并发症及器官衰竭发生率较高, 目前传统开放性手术已逐步被微创治疗所取代, 伴随着重症监护水平的提高, 这些措施减少了该病局部并发症的发生及降低了疾病病死率. 本文主要针对近几年AP局部并发症微创治疗相关研究进展进行综述.

1 急性胰周液体积聚和胰腺假性囊肿

急性胰腺炎最常见的局部并发症是急性胰周液体积聚(acute peripancreatic fluid collection, APFC). 液体均匀分布在发病前4 wk增多, 随着时间推移, 这些积液会自行吸收. 胰腺假性囊肿(pancreatic pseudocyst, PPC)为积液持续存在时间超过4 wk, 且有清晰的囊壁包裹. AP患者中PPC发生率可达20%^[4], 间质水肿性胰腺炎患者, 在发病后的4-6 wk, APFC可自行消退, 很少需要干预治疗^[5]. 一项纳入490名患者的荟萃分析比较了经皮引流与内镜引流对于有症状的胰周液体体积聚治疗效果, 结果显示内镜引流应该是症状性胰周液体体积聚的首选治疗方式, 其具有更好的临床成功率、更少的再干预率及较短的住院时间^[6].

PPC的介入指征取决于下述症状的出现, 包括胃流出道梗阻或腹痛^[7]. 当前指南并没有指出PPC需要多大才有必要进行干预治疗. 然而, 超过6 cm的假性囊肿通常会产生产生症状. 从发病开始, 大约需要4-6 wk时间囊肿才能包裹完整. 为减少并发症的发生, PPC的引流最好时机是在囊肿包裹完整后进行. Zhao等^[8]一项纳入255名患者的荟萃分析结果显示: 对于PPC治疗, 外科手术与内镜治疗相比, 手术组治疗成功率高于内镜组, 但内镜组治疗时间更短, 住院费用更低, 推荐PPC行内镜下经腔壁引流术是首选治疗, 也可行经皮穿刺置管引流术或手术治疗. 由于EUS引导下内镜下透壁引流可以引流胃肠道无隆起的胰周液体体积聚, 指南推荐初始行内镜透壁引流时, EUS引导优先于传统的透壁引流^[9]. 如果PPC与主胰管相通, 可能需要联合经十二指肠乳头引流. 然而, Yang等^[10]一项多中心研究结果显示: 对于PPC采取内镜下经腔壁引流联合经十二指肠乳头引流没有减少疾病的复发及增加患者获益, 该治疗方法目前仍存在争议性.

2 急性坏死物积聚和包裹性坏死

坏死性胰腺炎在发病前4 wk的积液为急性坏死性积液. 急性坏死物积聚(acute necrotic collection, ANC)包含数量不等的液体和坏死性物质. 坏死可仅累及胰腺实质, 但常伴有胰周坏死. 大约50%的患者, 坏死是位于胰腺外, 而无胰腺实质坏死^[11,12]. 通常在4 wk后, 急性坏死物积聚成熟并被包裹, 成为包裹性坏死(walled-off necrosis, WON)^[13]. 大多数坏死性胰腺炎患者可以采取保守治疗. 对无菌性坏死性胰腺炎进行引流可导致医源性感染, 从而增加额外的干预及手术相关的风险. 只有一小部分有持续症状患者考虑进行干预治疗. 例如腹痛, 胃肠道梗阻, 黄疸或发病后至少4-8 wk坏死囊壁“发育不全”. 一般不需要过早干预, 因为大部分会随时间推移自愈^[14,15].

在AP晚期发生感染性坏死性胰腺炎(infected necrotizing pancreatitis, INP)更多见, 但约25%的患者可在病程第一周即发生感染^[16]. 胰周坏死组织继发感染大多需要侵入性干预. 将近一半的INP患者, 继发感染通过CT上坏死灶中的气体结构变得明显可明确诊断^[13], 在诊断不明情况下, 可能需要经腹细针穿刺获得坏死组织的革兰染色或培养阳性结果. 然而, 细针穿刺缺点是有25%假阴性率^[17], 因此目前相关指南并不推荐常规进行细针穿刺活检^[3,9]. 当前指南推荐发病后至少4 wk再考虑行手术干预治疗, 将经皮穿刺置管引流推迟数周以后等到坏死组织形成囊壁时再行穿刺引流^[15,17,18]. 坏死组织液化及局限的过程使干预措施更加安全, 从而降低穿刺并发症的风险. 但具体干预时间仍无统一标准. 然而, Trikudanathan等^[19]回顾性研究发现, 胰腺炎在发病4 wk

以内, 此时胰腺包裹性坏死尚未形成, 内镜干预治疗更多的用于感染及器官衰竭患者, 且可降低患者死亡率. Chantarojanasiri等^[20]研究发现, 在接受早期引流的患者中, 穿孔或出血等并发症没有明显增加. Rana等^[21]研究发现对于INP患者经皮穿刺引流联合内镜引流及内镜下坏死组织清除术是安全有效的. 此外对于复杂WON或多处WON引流效果不佳时, 也可以采用多通道穿刺引流技术, 通过使用多个塑料支架^[16]或多个内镜贴壁金属支架(LAMS)^[22]来最大限度提高引流能力.

无论外科手术还是内镜微创都可以采用升阶梯(step-up approach)分阶段治疗. 包括经皮超声引导下穿刺引流术(percutaneous catheter drainage, PCD)、内镜超声引导透壁引流术(endoscopic ultrasound-guided transmural drainage, EUS-TD)、视频辅助腹膜后清创术(video-assisted retroperitoneal debridement, VARD)及内镜下坏死组织清创术(direct endoscopic necrosectomy, DEN)等. 目前常采用的胰腺炎外科升阶梯治疗即首先经PCD治疗, 必要时再实施VARD为主的外科手术治疗. 消化内镜升阶梯治疗即首先EUS-TD, 必要时再行内镜下坏死组织清创术(DEN)治疗. van Santvoort等^[23]进行的一项多中心随机试验发现, 在INP患者, 采取升阶梯治疗与开腹手术相比, 升阶梯治疗可减少主要并发症发生, 并可降低患者死亡率, 其主要并发症包括新发的多器官衰竭或多系统并发症, 内脏器官穿孔、肠痿、出血等. 这一差异在随访期间持续存在, 在升阶梯治疗组中, 没有增加额外侵入操作的需求^[24]. 然而van Brunschot等^[25]研究发现在内镜升阶梯治疗与外科升阶梯治疗相比, 两者死亡率及主要发病率没有显著差异, 但内镜升阶梯治疗患者平均住院时间较短, 发生肠痿更少. 综上所述, 升阶梯治疗(尤其是内镜升阶梯治疗)已逐渐成为INP的首选治疗方法. 对于大范围INP来说, 微创手术无法一次性彻底清除坏死组织, 反复多次微创手术疗效不佳. 在大量积液延伸至结肠旁沟或盆腔的患者, 可考虑EUS-TD和经皮导管引流联合治疗^[26].

近年来, 内镜治疗WON及INP进展迅速. 内镜贴壁金属支架(lumen-apposing metal stents, LAMS)于2011年研发, 作为传统使用的塑料支架替代品. LAMS与塑料支架相比有更大的管腔直径, 从理论上讲, 较大的直径可以改善坏死组织的引流, LAMS便于行内镜下经腔壁坏死组织切除术. Mussetto等^[27]研究显示, LAMS不仅可以作为胰腺坏死组织引流提供入口, 还可以用于肠道吻合及胆肠吻合的建立. 目前国内LAMS的临床应用经验仍较少. Bazerbach等^[28]研究显示, 对于WON的微创治疗, LAMS与塑料支架相比, 无论出血事件的发生, 支架阻塞、穿孔发生率LAMS均低于塑料支架, 但支架迁

移发生率要高于塑料支架. Bang等^[29]研究比较了内镜下LAMS和双猪尾塑料支架在感染和有症状的无菌WON患者中的疗效, 研究发现, 总手术次数的中位数、再入院次数和住院时间没有差别. 同时发现LAMS使用后3 wk如不移除, 相关不良事件发生率更高. 指南建议使用LAMS进行内镜下透壁引流应在4 wk内移除LAMS, 以最大限度地减少并发症的风险^[9]. Braden等^[30]研究发现, 随着EUS引导内镜支架置入可见度的提高, LAMS置入术可以在没有透视的情况下进行, 这使其作为危重病人的床旁干预措施. EUS引导内镜下透壁引流治疗WON, LAMS应用越来越广泛, 一项大型多中心研究结果显示: 与塑料支架相比, LAMS对于WON治疗具有更高的临床成功率, 更短的手术时间及更低的手术复发率^[31]. 美国一项大型多中心研究结果显示: 在放置LAMS时行DEN可减少WON的干预次数^[32].

3 胰管离断综合征

胰管离断综合征(disconnected pancreatic duct syndrome, DPDS)是指由任何原因导致的主胰管与消化道连接中断, 断端远侧胰腺分泌的胰液不能正常进入消化道, 在胰管断裂周围形成假性囊肿. 胰腺实质坏死经常导致胰管部分破裂或全部断开. 大约50%的急性坏死性胰腺炎患者会发生胰管破裂或断开^[33]. 胰管完整性可以通过MRCP来评估. 经内镜置入可跨越胰管断端的支架是目前比较有效的治疗手段. Arvanitakis等^[34]研究发现, 将跨腔支架留在原位可降低胰腺积液的复发. 指南推荐可长期留置双猪尾塑料支架进行液体引流, 这些支架可以无限期地留在原位, 以维持胃的内部引流^[9]对于胰管完全断裂的患者必要时可考虑行胰腺部分切除和胰管空肠吻合术.

4 血管并发症

近年来, SAP合并内脏静脉血栓发生率上升, Xu等^[35]研究发现, 其发病率可达16.6%, 其中门静脉、脾静脉和肠系膜静脉血栓发病率分别为6.2%, 11.2%和2.7%. 影像学检查发现在急性胰腺炎患者中约20%的患者有脾静脉血栓形成, 后期可出现门脉高压(胰源性), 导致胃底静脉曲张, 一旦破裂可引起消化道出血. 治疗上可以考虑行内镜下注射硬化剂、套扎或内镜下线圈联合氰基丙烯酸酯注射治疗, 也可考虑行脾切除术. 约4-10%病例出现腹腔出血或囊肿出血, 常因脾动脉、胃十二指肠动脉或胰腺周围血管受侵蚀, 胰腺假性动脉瘤破裂出血等引起, 血管造影可帮助及早发现出血部位, 因此动脉栓塞为主要治疗手段^[36,37]. 手术止血治疗多是在栓塞失败或造影未明确出血部位的情况下进行. Hines等^[38]研究结果提示

75%腹腔出血患者经导管动脉栓塞术或覆膜支架置入术治疗有效。

5 消化道并发症

SAP患者病程后期容易出现消化道瘘^[39], Jiang等^[40]研究显示其发病率在12.8%, 可累及胃、十二指肠、空肠、回肠、结肠, 好发部位为十二指肠与结肠, 可能与富含胰酶消化液渗出, 肠道血管血栓形成导致肠管缺血坏死或感染侵蚀有关。此外, 手术干预也可导致消化道瘘。瘘管的处理方法受瘘管位置的影响。Kochhar等^[39]研究发现大部分上消化道瘘可随时间推移自然愈合, 结肠瘘常需积极干预, 且发生结肠瘘的患者死亡率更高。基本治疗原则为保持消化液引流通畅, 如经皮穿刺引流或持续负压冲洗, 结肠瘘腹腔污染严重, 常需要肠造瘘术治疗。SAP合并十二指肠瘘, 如果保守治疗感染仍不能控制, 腹腔镜下腹膜后清创术为有效治疗方法。

6 结论

综上所述, 急性胰腺炎局部并发症不仅导致患者的住院时间、医疗费用大大增加, 也导致该病的病死率明显上升。近年来随着AP治疗理念的转变, 对于AP局部并发症的治疗已由传统的开腹清创术转变为微创治疗为主的多学科综合救治模式, 但目前关于AP局部并发症的治疗尤其是微创治疗最佳时机仍存在争议, 关于内镜下支架的使用仍存在弊端, 仍需大样本临床试验来进一步研究改进。目前我国对于急性胰腺炎局部并发症的干预策略不同医疗中心之间仍存在差异性, 微创治疗技术和理念仍需进一步提高和普及。对于感染坏死性胰腺病变范围广及部位复杂时, 微创治疗可能需要多次, 多部位进行, 甚至需行外科开腹手术治疗, 避免错过最佳治疗时机, 从而使患者获得更大的临床获益。

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科学编辑: 张砚梁 制作编辑: 张砚梁



ISSN 1009-3079 (print) ISSN 2219-2859 (online) DOI: 10.11569 © 2021 Baishideng Publishing Group Inc. All rights reserved.

• 消息 •

《世界华人消化杂志》正文要求

本刊讯 本刊正文标题层次为 0 引言; 1 材料和方法, 1.1 材料, 1.2 方法; 2 结果; 3 讨论; 4 参考文献. 序号一律左顶格写, 后空 1 格写标题; 2 级标题后空 1 格接正文. 以下逐条陈述: (1) 引言 应包括该研究的目的和该研究与其他相关研究的关系. (2) 材料和方法 应尽量简短, 但应让其他有经验的研究者能够重复该实验. 对新的方法应该详细描述, 以前发表过的方法引用参考文献即可, 有关文献中或试剂手册中的方法的改进仅描述改进之处即可. (3) 结果 实验结果应合理采用图表和文字表示, 在结果中应避免讨论. (4) 讨论 要简明, 应集中对所得的结果做出解释而不是重复叙述, 也不应是大量文献的回顾. 图表的数量要精选. 表应有表序和表题, 并有足够具有自明性的信息, 使读者不查阅正文即可理解该表的内容. 表内每一栏均应有表头, 表内非公知通用缩写应在表注中说明, 表格一律使用三线表(不用竖线), 在正文中该出现的地方应注出. 图应有图序、图题和图注, 以使其容易被读者理解, 所有的图应在正文中该出现的地方注出. 同一个主题内容的彩色图、黑白图、线条图, 统一用一个注解分别叙述. 如: 图 1 萎缩性胃炎治疗前后病理变化. A: …; B: …; C: …; D: …; E: …; F: …; G: … 曲线图可按 ●、○、■、□、▲、△ 顺序使用标准的符号. 统计学显著性用: ^a $P < 0.05$, ^b $P < 0.01$ ($P > 0.05$ 不注). 如同一表中另有一套 P 值, 则^c $P < 0.05$, ^d $P < 0.01$; 第 3 套为^e $P < 0.05$, ^f $P < 0.01$. P 值后注明何种检验及其具体数字, 如 $P < 0.01$, $t = 4.56$ vs 对照组等, 注在表的左下方. 表内采用阿拉伯数字, 共同的计量单位符号应注在表的右上方, 表内个位数、小数点、±、- 应上下对齐. “空白”表示无此项或未测, “-”代表阴性未发现, 不能用同左、同上等. 表图勿与正文内容重复. 表图的标目尽量用 t/min , $c/(\text{mol/L})$, p/kPa , V/mL , $t/^\circ\text{C}$ 表达. 黑白图请附黑白照片, 并拷入光盘内; 彩色图请提供冲洗的彩色照片, 请不要提供计算机打印的照片. 彩色图片大小 $7.5\text{ cm} \times 4.5\text{ cm}$, 必须使用双面胶条黏贴在正文内, 不能使用浆糊黏贴. (5) 致谢 后加冒号, 排在讨论后及参考文献前, 左齐.



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ISSN 1009-3079

