

术后消化道反流性疾病的现状和治疗

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基金项目: 国家自然科学基金资助项目, No. 81572350.

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收稿日期: 2016-02-14
修回日期: 2016-03-30
接受日期: 2016-04-05
在线出版日期: 2016-06-18

Post-surgical gastrointestinal reflux disease: Status quo and treatment

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Supported by: National Natural Science Foundation of China, No. 81572350.

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Received: 2016-02-14
Revised: 2016-03-30
Accepted: 2016-04-05
Published online: 2016-06-18

Abstract

Reflux is a common and tricky morbidity after

gastrointestinal surgery which is caused by the destruction of physiological anti-reflux barriers, greatly affecting patients' postoperative quality of life. Gastroenterologists are now actively trying very hard to explore feasible, effective, and safe anti-reflux approaches. Conservative medical treatment, typically with proton pump inhibitors, is easily accepted by patients, however, its long-term adverse events are noteworthy. In the surgical aspect, laparoscopic anti-reflux surgery is gaining more and more popularity, after the first case of fundoplication. Besides, other operations, such as bariatric surgery, pediatric surgery, and pulmonary transplantation, are also frequently complicated by post-operative digestive reflux. Herein we systematically review the status quo and treatment modalities for post-surgical reflux disease, with the hope to facilitate surgeons to cope with this challenging issue appropriately.

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Key Words: Post-operational gastrointestinal reflux; Status quo; Conservative medical treatment; Surgical treatment

Huang L, Xu AM. Post-surgical gastrointestinal reflux disease: Status quo and treatment. *Shijie Huaren Xiaohua Zazhi* 2016; 24(17): 2601-2607 URL: <http://www.wjgnet.com/1009-3079/full/v24/i17/2601.htm>
DOI: <http://dx.doi.org/10.11569/wcjd.v24.i17.2601>

摘要

反流是消化道手术后一种常见而棘手的并发症, 由多种生理抗反流屏障被破坏所致。其严重地影响着患者的术后生活质量。目前,

背景资料

反流是消化道手术后一种常见而棘手的并发症, 严重地影响着患者的术后生活质量, 其是食管癌和食管胃结合部腺癌的高危因素。以抑酸为主的内科保守治疗容易被患者接受, 然而, 其远期不良反应不容忽视。在手术处理方面, 腔镜抗反流手术越来越受到外科界欢迎。

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■ 研究前沿

国内外学者均对术后反流发生机制进行了研究, 应积极加强相关多中心、大样本、严格纳入排除标本的前瞻性临床研究, 另外, 循证医学研究和相关基础机制研究亦不可忽视。关于不同组分反流液的具体致病作用及其影响因素尚存争议, 而其对术后是否应该抑酸等非手术治疗方案的选取具有重要意义, 故有必要进一步开展不同胃切除和重建术式前后反流液成分、酸碱度及其与炎症、症状严重程度间相关性分析等。此外, 应加强开放和腔镜抗反流手术的临床对照研究。

胃肠病学家正努力积极探索可行安全而有效的抗反流方法。以质子泵抑制剂为代表的内科保守治疗容易被患者接受, 然而, 其远期不良反应不容忽视。在手术处理方面, 自从第一例胃底折叠术的成功实施, 腔镜抗反流手术越来越受到外科界欢迎。此外, 其他手术如减重手术、小儿外科手术、肺移植术等术后亦常并发消化道反流。这里, 我们系统性回顾论述术后反流性疾病的现状和治疗措施, 希望能有助于外科医生正确处理这个挑战性的难题。

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关键词: 术后消化道反流性疾病; 现状; 内科保守治疗; 手术治疗

核心提示: 消化道术后反流性疾病是外科界一常见而棘手的难题。对于此类患者, 内科保守治疗和外科处理各有优缺点, 其选择尚存争议。其中, 质子泵抑制剂的使用受争议, 而腔镜外科备受重视。其他手术术后亦常并发消化道反流。

黄雷, 徐阿曼. 术后消化道反流性疾病的现状和治疗. 世界华人消化杂志 2016; 24(17): 2601-2607 URL: <http://www.wjgnet.com/1009-3079/full/v24/i17/2601.htm> DOI: <http://dx.doi.org/10.11569/wjcd.v24.i17.2601>

0 引言

反流是消化道手术后一种常见而棘手的并发症, 其严重地影响着患者的术后生活质量。术后消化道反流包括胃-食管反流(gastroesophageal reflux disease, GERD)、十二指肠-胃反流等。反流液中胃酸、胆汁酸、胆红素和各种消化酶作用于残胃、食管黏膜可致局部炎症、化生、不典型增生甚至癌变^[1]。世界范围内胃癌(gastric cancer, GC)发病率有下降趋势, 然而食管胃结合部腺癌(adenocarcinoma of gastroesophageal junction, AEG)的发生率却持续上升^[2,3]。GERD是食管癌和AEG的高危因素。术后反流可显著增高Barrett食管的发生率进一步导致重度不典型增生和癌变^[4], 其中氧化应激可起重要作用^[5]。不同的手术方式术后发生反流的原因不同。总的来说, 术后发生反流的原因可能有: (1)上消化道连续性切断, 贲门括约肌丧失; (2)残胃排空延迟, 十二指肠逆蠕动; (3)胃腔部分切除或移位后缩小变形, 残胃变成管道, 胃的储存功能减弱或

消失; (4)术后幽门受牵拉而功能减弱, 幽门成形或切除后失去了其“关卡”作用; (5)食管下括约肌(lower esophageal sphincter, LES)长度及压力均短于和低于正常, 且食管中远段干涩、蠕动振幅降低, 食管异常收缩增多; (6)迷走神经远端切断, 胃张力下降; (7)吻合口的贯通作用及胸腔腹腔压力差的存在; (8)膈肌角固有的解剖结构被破坏等。目前, 胃肠病学家正努力积极探索可行安全而有效的抗术后反流方法。质子泵抑制剂(proton pump inhibitors, PPIs)于20世纪90年代应用于临床, 其他以抗酸为主的抗GERD药物有牛奶增稠剂, 酸缓冲剂, 促胃肠动力剂和海藻酸钠制剂等。以抑酸为主的内科保守治疗容易被患者接受, 然而, 其远期不良反应不容忽视。在手术处理方面, 腔镜抗反流手术越来越受到外科界欢迎。对于此类患者, 内科保守治疗和外科处理各有优缺点, 其选择尚存争议。这里, 我们回顾综述术后反流性疾病的现状和治疗措施, 希望能有助于外科医生正确处理这个挑战性的难题。

1 胃手术后的反流

胃切除术后患者常发生反流, 严重影响生活质量^[6]。胃切除和消化道重建类型可影响术后胆汁反流。反流液中胆汁酸浓度和总细菌计数与食管胃黏膜的病理改变有关。胃切除患者是研究胆汁反流和胃酸抑制对食管胃黏膜改变影响的良好模型。在先前接受过上消化道或胆道手术的患者, 胃排空延迟与反流症状相关^[7]。Taha等^[8]研究显示, 反流和Barrett食管的发生率和严重程度在胃手术后尤其在迷走神经切断术后长时间内并未增高, 其与胆汁反流无关。Zhang等^[9]报道高选择性迷走神经切断(highly selected vagotomy, HSV)可有效地防治胃切除术后胆汁反流, 从而使食管胃生理功能保持稳定。GERD除了典型的反酸、烧心等症状外, 常伴有食管外的非特异性症状(如声音嘶哑、咳嗽、气喘等)。食管近端pH检测可鉴别此类症状的原因, 然而却不能有效区别抗反流手术的成功与否^[10]。食管和胃局部的pH值对远期症状没有良好的预测作用。

1.1 胃手术后反流的内科治疗 GC患者接受胃切除术后是否需要抑酸尚存争议。1994年世界卫生组织(World Health Organization, WHO)/国际癌症研究机构(International Agency for

Research on Cancer, IARC)将幽门螺旋杆菌(*Helicobacter pylori*, *H. pylori*)定为 I 类致癌原, 随后根除*H. pylori*的药物大量应用于临床, 尤其是以奥美拉唑为代表性药物的PPIs. PPIs是一种非常有效的药物, 其作用机制是阻断胃壁细胞分泌管上 H^+/K^+-ATP 酶的活性从而阻断任何刺激引起的胃酸分泌. 然而, 其会引起胃壁细胞增生、腺囊肿、高胃泌素血症及胃底腺息肉等不良反应. 长期使用PPIs还会增加沙门氏菌、弯曲杆菌和梭状芽孢杆菌等的感染风险^[11-15]. PPIs增加细菌感染风险普遍认为是与其抑制胃酸的分泌导致胃中的pH值增加有关. 并且, 由于术中迷走神经干或其分支常被切断, PPIs的使用利弊就更难以确定. 目前临床医师对PPIs使用指征把握不准而大量不规范泛滥使用PPIs. 在澳大利亚、爱尔兰和英国使用PPIs的患者中, 分别有63%、33%和67%的患者没有按照标准使用该药^[16]. 对于需要长期使用PPIs的患者, 建议定期行胃镜检查避免胃和食管胃结合部(esophagogastric junction, EGJ)肿瘤的发生^[17]. 而我们的研究结果^[18]显示, 胃手术后胃内pH大部呈弱酸性, 且均高于术前水平. 术后反流普遍发生, 年老患者有更严重的反流, 反流症状与患者体质指数, 胆红素和总胆汁酸水平相关, 而与pH值无关. 因而, 术后没有必要进一步碱化胃肠液. 我们并不推荐长期使用PPIs进行抗术后反流治疗.

1.2 胃手术后反流的外科和介入处理 有些术后GERD患者不愿终身服药. 一个12年的前瞻性研究^[19]表明, 抗反流手术(anti-reflux surgery, ARS)比奥美拉唑可更有效控制病情, 但胃底折叠术后仍有少部分患者症状复发或持续. 修复生理抗反流机制的ARS对防止反流复发非常有效. 术后患者嗝气功能虽可保留, 但往往有所减弱, 进而导致胃和直肠胀气^[20]. 即使对反流患者施行ARS, 术后食管和贲门部腺癌的发生率仍然升高^[21]. 大鼠模型表明GM-CSF全细胞肿瘤疫苗可有效诱发对抗皮下接种的肿瘤的强的免疫反应, 并保护动物使其不发生手术所致反流而进一步导致的食管癌^[22]. 食管癌患者中, 在EGJ放置金属支架常可导致反流性症状. 此时, 加用PPI和换用抗反流支架可取得类似的效果, 但由于后者较昂贵而不推荐使用^[23,24].

1.3 胃手术后反流的腔镜处理 随着腹腔镜手术

的普及, ARS种类越来越多. 对于GERD患者, 相比PPIs治疗, 腹腔镜抗反流手术(laparoscopic ARS, LARS)可在中长期更好地控制食管酸暴露^[25]. 在教学和社区医院, Nissen胃底折叠术因其可缩短住院和术后恢复时间且有较低的术后并发症和死亡率而被广泛应用. 其可显著减少术后酸和弱酸液体反流, 却不能很好控制气体反流. 三种机制可解释此现象: 双重高压区的废除(食管裂孔疝), 暂时性食管下括约肌松弛(transient lower oesophageal sphincter relaxations, TLOSRS)的频率减少, 以及TLOSRS与反流的相关性减小^[26]. 短期和长期内部分和完全腹腔镜胃底折叠术在反流控制效果方面没有明显区别^[27]. 一个国外三级甲等医院调查^[28]显示, 尽管大部分患者对腹腔镜下胃底折叠术后效果很满意, 他们术后仍持续使用抗反流药物. 然而, 部分患者施行此种手术后症状并未改善, 且此种术式的长期并发症不可忽视, 如气体膨胀综合征、吞咽困难、腹泻、GERD复发, 甚至死亡等^[29]. 这些可能导致再次手术. Yang等^[30]报道对行胃底折叠术后吞咽困难的患者施行内镜下扩张或者修复手术, 约2/3患者可获得满意效果. ARS后若反流长期持续存在则可诱发食管腺癌^[31]. 复发或难治性GERD的临床表现不一, 导致ARS失败的原因很难察觉且不易处理. Bais等^[32]报道再次ARS可增加LES压力和减少反流次数, 从而有着良好和持续的控制反流症状和反流性食管炎的效果, 甚至可取得和初次手术类似的疗效. ARS后复发性GERD有时很难处理, 尤其在药物治疗无效的患者. 对于此类患者, 大部分需行再次行手术治疗, McClusky等^[33]报道内镜下射频能量传递至食管下括约肌(lower esophageal sphincter, LES)治疗手段(Stretta处理)可显著减轻症状, 提高患者生活质量. Chen等^[34]报道Belsey Mark IV胃底折叠术对难治性复发性反流是有效且可被耐受的. 对于射频消融术或腔内折叠术治疗失败的GERD患者, LARS可起到很好的作用. 然而, LARS对于行生物聚合物注入术的患者却不适用^[35]. 经口腔胃底折叠术(transoral incisionless fundoplication, TIF)通过透壁的紧固件制造全层的食管胃折襞而可有效地治疗GERD. 如果不成功, 则修正LARS(revision LARS, rLARS)是一种安全有效的补救方法^[36]. Shitrit等^[37]报道腔镜下可调节胃束带术(laparoscopic AGB, LAGB)

■ 相关报道

目前, 胃肠病学专家正努力积极探索可行安全而有效的抗术后反流方法. 质子泵抑制剂于20世纪90年代应用于临床, 其他以抗酸为主的抗反流药物有牛奶增稠剂, 酸缓冲剂, 促胃肠动力剂和海藻酸钠制剂等. 以抑酸为主的内科保守治疗容易被患者接受, 然而, 其远期不良反应不容忽视. 在手术处理方面, 腹腔镜抗反流手术越来越受到外科界欢迎. 对于此类患者, 内科保守治疗和外科处理各有优缺点, 其选择尚存争议.

■ 创新盘点

消化道反流为内科一常见多发病。在外科系统中, 多种手术术后亦常并发消化道反流, 且由于生理抗反流屏障的结构常被破坏, 其治疗成为一棘手难题。内科外科处理手段对术后反流均有一定疗效, 但应权衡各治疗措施的利弊。

和腹腔镜下袖状胃大部切除术(laparoscopic sleeve gastrectomy, LSG)也是安全有效的, 而LSG比LAGB术后咳嗽发生率低。再次手术虽可在大部分患者中起到控制反流和症状的作用^[38], 但其并发症不可忽视^[39]。

2 非胃手术后的反流

2.1 减肥手术后的GERD及治疗 肥胖是GERD的易感因素。Roux-en-Y胃旁路手术(Roux-en-Y gastric bypass, RYGB)是患有胃食管反流性疾病的病态肥胖人群的最佳手术治疗手段, 其与可调节胃束带术(adjustable gastric banding, AGB)相比具有更加术后胃肠动力, 更优酸反流控制等优点^[40]。而Korenkov等^[41]报道减肥手术并不能有效地减轻病态肥胖患者术后GERD症状。仍有一部分患者手术后患有顽固性或复发性的GERD。首次抗反流手术失败的肥胖患者(BMI>30 kg/cm²)是胃肠外科医生的一个难题。对于此类患者, 再次施行胃底折叠或胃旁路手术是安全的^[42]。残胃胃底折叠术或用射频处理LES可获得一定疗效, 然而较难实施; Pescarus等^[43]报道腹腔镜Hill手术是安全有效耐久的。Raftopoulos等^[44]报道修正的腹腔镜下Roux-en-Y胃旁路手术(laparoscopic RYGB, LRYGB)虽然可能具有更多的术后并发症且操作起来更困难, 但其对于复发GERD的肥胖患者的治疗却是可行且有效的, 且能使肥胖加重的患者体质量得到控制和减轻合并症。对于初次ARS失败的难治性GERD肥胖患者也可施行食管空肠吻合口附近Roux-en-Y吻合术(Roux-en-Y near esophagojejunostomy, RNYNEJ), 然而其并发症不可忽视。不过, 大部分患者可获得满意的症状控制和改善, 部分患者甚至可以得到体质量减轻、合并症改善等益处^[45]。

2.2 小儿外科术后的GERD及治疗 在小儿外科, 食管闭锁(esophageal atresia, EA)伴或不伴气管食管瘘(tracheoesophageal fistula, TEF)手术修复后常并发GERD, 并可进一步导致吻合口狭窄等并发症。然而, 此方面的处理尚未达成共识^[46]。在术后第1年, EA±TEF伴有症状GERD患者的GERD严重程度和发生率比无症状患者显著高。核素显像显示近端反流与有症状GERD有关^[47]。在儿童胃底折叠术可有效地降低术后GERD发生率而不影响食管动力^[48]。对神经功能缺损(neurological impairment, NI)的

患儿施行胃造口置饲喂管术可改善其因经口进食困难所致的营养不良发育缓慢等症状, 但其可导致或加重患儿的GERD^[49]。所致的GERD在施行胃底折叠术前均很难被动态24 h pH监测所甄别, 由于广泛的胃肠道无障碍, 非酸反流, 和通过鼻胃管进行肠内营养而导致的近端反流。对于此类患者, 多通道阻抗pH值测量(multichannel impedance-pH measurement, pH/MII)可有效诊断GERD且能鉴别其亚型^[50]。

2.3 终末期肺病患者肺移植术后的GERD及治疗 GERD在终末期肺病患者施行肺移植术前很常见, 并可在肺移植术后导致闭塞性细支气管炎。肺移植患者比一般GERD患者更容易发生近端反流, 尽管两者有相似的测压结果, 食管炎和Barrett食管发生率。在肺移植患者, 无症状反流导致中性粒细胞增多, 可进一步导致移植物功能障碍和死亡, 且可在术后早期发生。此类患者应在术后1 mo内常规性地进行反流/误吸评估^[51]。如果在支气管肺泡灌洗液(bronchoalveolar lavage fluid, BALF)中误吸标志物(如胆盐, 胃蛋白酶等)升高, 则可早期施行胃底折叠术。与一般GERD患者相比, LARS不增加合并GERD的肺移植患者的并发症率和死亡率^[52]。对患有GERD的肺移植患者施行LARS可影响免疫功能而避免闭塞性细支气管炎。LARS可恢复肺白细胞亚群的生理平衡, 并减少BALF中的促炎介质, 从而调节肺部的炎症微环境^[53], 进一步改善移植物功能并延长其寿命^[54]。

2.4 其他手术后反流 反流可导致胆道术后(如胆囊切除术, 胆总管十二指肠吻合术, 内镜下乳头括约肌切开术等)患者的消化不良症状。Fountos等^[55]报道红霉素可将此类反流降至正常水平。在脊柱外科中, 与后路椎管减压术相比, 经颈椎前路减压融合术在术后早期有更频繁且更严重的GERD样症状^[56]。

3 结论

消化道反流为手术后常见的并发症, 为消化外科界一大难题。我们不推荐长期内科使用抑酸剂以控制症状, 因其有远期致癌效应。我们团队的一项尚待接受研究表明长期使用以奥美拉唑为代表的PPIs可显著促进实验小鼠EGJ不典型增生乃至癌变的发生率。内镜和介入治疗创伤较小, 但其效果难以得到保证且应用受限,

其实施应严格把握指征. 外科治疗中, LARS因其微创的有点而得到普遍应用和研究. 然而, 我们不能忽视传统ARS的作用. 我们认为应加强开放和腔镜ARS的临床对照研究. 此外, 根据我们的临床实践, 让术后患者嚼口香糖和进餐后慢步行走亦为很好控制术后反流症状的方法.

国内外学者均对GERD发生机制进行了研究, 但其机制尚不完全清楚, 因此应当重视相关基础研究. 不同文章对不同手术方式报道详细程度不一、对同一方式亦存不同见解, 我们认为应积极加强相关多中心、大样本、严格纳入排除标本的前瞻性临床研究, 合理控制干扰因素, 使结果更具真实、可靠性, 另外, 循证医学研究亦不可忽视. 国内外学术界应加强交流. 关于不同组分反流液的具体致病作用及其影响因素尚存争议, 而其对术后是否应该抑酸等非手术方案的选取具有重要意义, 故有必要进一步开展不同胃切除和重建术式前后反流液成分、酸碱度及其与炎症、症状严重程度间相关性分析等.

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应用要点

消化道反流为手术后常见的并发症, 为消化外科界一大难题. 不推荐长期内科使用抑酸剂以控制症状, 因其远期致癌效应. 内镜和介入治疗创伤较小, 但其效果难以得到保证且应用受限, 其实应严格把握指征. 外科治疗中, 腔镜手术因其微创的优点而得到普遍应用和研究. 然而, 我们不能忽视传统抗反流手术的作用.

■名词解释

生理性抗反流屏障: 指在食管和胃交接的解剖结构, 包括食管下括约肌(lower esophageal sphincter, LES)、膈肌脚、膈食管韧带、食管与胃底间的锐角(His角)等, 上述各部分的结构和功能上的缺陷均可造成胃食管反流, 其中最主要的是LES的功能状态; 术后胃食管反流: 手术后胃食管腔因过度接触或暴露于胃液而引起的临床胃食管反流症和食管黏膜损伤的疾病。胃食管反流及其并发症的发生是多因素的, 其中包括食管本身抗反流机制的缺陷, 如食管下括约肌功能障碍和食管体部运动异常等; 也有食管外诸多机械因素的功能紊乱。

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同行评价

术后消化道反流性疾病是非常棘手的问题,选题对临床具有积极意义。此篇文章较新颖,参考了国内外的许多资料,对我国的大部分医院有指导意义。

编辑: 于明茜 电编: 都珍珍





Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton,
CA 94588, USA
Fax: +1-925-223-8242
Telephone: +1-925-223-8243
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ISSN 1009-3079

