

# 成人非复杂性急性阑尾炎治疗进展

傅俊豪, 张浩\*

重庆医科大学附属第二医院消化内科, 重庆

收稿日期: 2022年11月7日; 录用日期: 2022年12月1日; 发布日期: 2022年12月14日

## 摘要

急性阑尾炎是由阑尾腔阻塞(主要包括淋巴结增生和粪石阻塞)后继发感染形成的疾病。近年来,随着相关随机对照试验的开展以及对阑尾炎治疗方式的不断探索,急性阑尾炎的治疗方式取得了一定的进展。阑尾切除术能够从根源切除病灶并杜绝阑尾肿瘤的发生,但术后并发症较多。单用抗生素治疗能明显缩短住院时间,减少并发症并且成本较低,但有一定的失败率及较高的复发率。内镜逆行阑尾炎治疗属于微创手术,与阑尾切除术一样能立即缓解腹痛,有着极高的治疗成功率,极低的复发率及并发症发生率。在此,我们将对非复杂性急性阑尾炎的治疗方式进行介绍与讨论,以期临床决策提供一定的参考。

## 关键词

非复杂性急性阑尾炎, 阑尾切除术, 抗生素, 内镜逆行阑尾炎治疗

# Progress in the Treatment of Uncomplicated Acute Appendicitis in Adults

Junhao Fu, Hao Zhang\*

Department of Gastroenterology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing

Received: Nov. 7<sup>th</sup>, 2022; accepted: Dec. 1<sup>st</sup>, 2022; published: Dec. 14<sup>th</sup>, 2022

## Abstract

Acute appendicitis is a disease caused by secondary infection after obstruction of the appendiceal cavity, mainly including lymph node hyperplasia and obstruction of the fecalith. In recent years, with the development of relevant randomized controlled trials and the continuous exploration of the treatment of appendicitis, the treatment of acute appendicitis has made some progress. Ap-

\*通讯作者。

pendectomy can remove the lesions from the root and prevent the occurrence of appendiceal tumors, but there are many postoperative complications. Antibiotic therapy alone can significantly shorten the length of hospital stay, reduce complications and cost less, but it has a certain failure rate and a high recurrence rate. Endoscopic retrograde appendicitis treatment is a minimally invasive surgery, which can relieve abdominal pain immediately as appendectomy. It has a high success rate of treatment and a very low recurrence rate and complication rate. In this article, we will introduce and discuss the treatment of uncomplicated acute appendicitis, in order to provide some reference for clinical decision-making.

## Keywords

Uncomplicated Acute Appendicitis, Appendectomy, Antibiotics, Endoscopic Retrograde Appendicitis Treatment

Copyright © 2022 by author(s) and Hans Publishers Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## 1. 引言

急性阑尾炎(acute appendicitis, AA)是急性腹痛最常见的原因之一,也是因急腹症入院的年轻患者最常见的疾病。穿孔率从 16%到 40%不等[1],与未穿孔的 AA 相比,阑尾穿孔会导致死亡率增加。阑尾切除术从过去到现在一直是治疗各型阑尾炎的标准治疗方式,虽有很高的治疗成功率,但其也存在术后并发症较多的缺陷。近年来,随着抗生素与手术治疗阑尾炎的随机对照试验(randomized controlled trial, RCT)的陆续开展[2] [3] [4],越来越多的研究显示抗生素疗法具有较高成功率,较低的成本及较短的住院时间,并被较多研究者提议作为非复杂性急性阑尾炎(uncomplicated acute appendicitis, UCAA)的一线治疗方案。然而,不少研究提示单用抗生素保守治疗有高达近 40%的复发率,且治疗失败率与阑尾腔直径、粪石阻塞等因素密切相关。针对 UCAA 的治疗,10 年前刘冰熔教授首次提出内镜下逆行阑尾炎治疗术(endoscopic retrograde appendicitis treatment, ERAT),该方式目前主要在中国开展。不少临床研究显示其治疗成功率高达 97%,且复发几率低,并发症少,还能保留阑尾的生理功能。现阶段,国际上针对非复杂性急性阑尾炎的治疗方式尚未统一。本文就非复杂性急性阑尾炎的治疗进展进行综述。

## 2. 非复杂性急性阑尾炎的定义

现代诊断策略是首先确认或排除阑尾炎的诊断,然后在怀疑阑尾炎时对简单和复杂的疾病进行分层。1986 年 Alvarado 通过 AA 病例的回顾性分析得出满分 10 分的诊断标准,≥7 分考虑阑尾炎的可能性比较大。最近的综述发现 CT 检测下的阑尾炎特点包括阑尾腔扩张(≥7 毫米);阑尾壁增厚、强化或两者都有[5]。而非复杂性阑尾炎指单纯的膨胀性阑尾炎,没有坏疽或坏死,未形成穿孔及盆腹腔脓肿,表现为轻微的炎症、化脓性炎或蜂窝织炎[6]。

## 3. 治疗方式

### 3.1. 阑尾切除术

Fitz 于 1886 年首次描述了急性阑尾炎这种疾病,这种疾病在当时通常是致命的,由于缺乏抗生素,必须通过手术迅速切除阑尾,以避免危及生命的感染、败血症和死亡。自从 19 世纪外科医生开始进行阑

尾切除术以来, 手术切除阑尾一直是治疗阑尾炎的金标准, 但切除正常阑尾的风险仍在 8%~15%的病例中发生[7] [8] [9]。阑尾切除术除了较高的有效率, 还提供了阑尾明确的组织学和阑尾外病理的机会[10] [11] [12]。在 Renteria 等人[10]对接受阑尾切除术作为 AA 主要治疗的老年人(平均年龄 66 岁)的研究中发现恶性肿瘤发生率为 3%, 年轻人群(平均年龄 39 岁)中恶性肿瘤发生率为 1.5%。Kwan [11]在 1492 例阑尾切除术后病理结果的回顾性调查中发现关于阑尾肿瘤病变, 类癌肿瘤是最常见的, 在该研究中占病例的 0.5%, 这也与既往文献显示的比例(0.3%~0.9%)相当。是否对所有阑尾切除标本进行组织病理学评价以进一步评估肿瘤风险一直存在争议(因为不这样做可能是降低成本的一种方法), 但仍然是一种最佳实践建议, 主要是因为它能使约 1%的患者意外发现恶性肿瘤, 其中最常表现为类癌、腺癌或粘液性囊腺瘤[12]。但也有较多的研究表明切除阑尾的方式并不能得到一致支持。Masahata 的研究[13]提示阑尾中的淋巴器官是产生 IgA 细胞并迁移到大肠的主要组织, 分泌的 IgA 被证明可以控制肠道微生物稳态。Randal Bollinger 的研究[14]指出阑尾是一种在与其上皮粘膜相关的生物膜中维持正常肠道细菌储备的结构。阑尾的结构有望增强生物膜形成对共生菌的保护作用。Meng Wen 在结直肠癌的筛查中[15]指出阑尾作为淋巴器官, 在结肠癌发生中起着保护作用。此外, Andersson Roland E [16]研究显示有阑尾切除术史的患者发生克罗恩病的风险增加。故对于阑尾是去是留, 目前尚存争议。

当前的临床实践及相关的对照研究均表明手术治疗的方式中, 腹腔镜阑尾切除术(laparoscopic appendectomy, LA)是最有效的手术治疗, 与开腹阑尾切除术(open appendectomy, OA)相比, 其伤口感染发生率和干预后发病率较低, 住院时间较短, 生活质量评分更高[17] [18] [19]。2020 年更新的世界急诊外科学会阑尾炎治疗指南推荐: 对于非复杂和复杂的急性阑尾炎, 腹腔镜阑尾切除术优于开腹阑尾切除术, 腹腔镜阑尾切除术在减轻疼痛、降低手术部位感染发生率、缩短住院时间、尽早返回工作岗位、整体成本和更好的生活质量评分方面优于开腹阑尾切除术。并建议 UCAA 患者术后不要使用抗生素[20]。Xue Chaorong 等[21]在基于随机对照试验的高水平 meta 分析中显示虽然单孔腹腔镜与三孔腹腔镜在疗效上没有显著差异, 但由于单孔腹腔镜的手术时间明显长于三孔腹腔镜, 所需的镇痛剂量也更高, 并发症发生率相似, 恢复相当, 因此不支持单孔腹腔镜的应用, 这与 Jonathan T. Carter 等[22]报道的前瞻性随机对照试验及 Dayun Wang 等人[23]发表的 meta 分析的研究结果一致。有趣的是, Kang Byung Mo 等人[24]开展的随机对照试验也同样表明单孔腹腔镜有更长的手术时间和更长的住院时间, 但功能恢复得也更晚。对于接受阑尾切除术的急性阑尾炎患者, 有不同的残端闭合技术(包括内镜吻合器或内镜袪、残端结扎或残端内翻等)。虽然早期的研究最初报道了常规使用内镜吻合器在并发症和手术时间方面的优势, 但最近的研究一再表明, 内镜吻合器和内镜袪残端闭合在术后或内部并发症方面没有差异[25]。Van Rossem 等进行的多中心前瞻性观察研究表明, 在比较残端内环或内镜吻合器时, 感染并发症发生率不受阑尾残端闭合方式的影响[26]。Qian 等纳入 11 项 RCT 进行系统回顾和 meta 分析表明单纯结扎组与残端倒置组术后发热、感染情况相似, 但单纯结扎组手术时间短, 术后肠梗阻发生率低, 术后恢复快。临床结果显示, 无论是开腹手术还是腹腔镜手术, 单纯结扎术明显优于残端倒置术[27]。

2018 年 van Dijk S T 等[28]发表的一项 meta 分析表明, 延迟阑尾切除术治疗 UCAA 并不是发展为复杂阑尾炎的危险因素, 而且不会增加术后并发症。这些结果提示了外科医生可以将非复杂性急性阑尾炎患者的阑尾切除术推迟一整夜。

### 3.2. 抗生素保守治疗

1995 年起国际上就已开展关于阑尾炎抗生素治疗的随机对照试验。根据阑尾炎切除后的病理活检显示, 切除阑尾中的细菌生长由需氧和厌氧细菌混合而成, 最常见的是大肠杆菌和拟杆菌[29], 阑尾炎作为感染性疾病, 针对性抗感染治疗被证明同样是可行的。既往有研究报道, 在 1 年的随访期间, 抗生素保

守治疗的成功率约 73%，大多数随机接受抗生素治疗的 UCAA 患者不需要阑尾切除术[30] [31]。根据 APPAC 试验的 5 年随访结果显示，在最初使用抗生素治疗的非复杂性急性阑尾炎患者中，晚期复发的可能性为 39.1%。与阑尾切除术组相比，抗生素组的总并发症发生率明显降低(6.5% vs 24.4%)。这一长期随访结果支持抗生素治疗联合抗生素作为 UCAA 手术的替代方案的可行性[32]。LoVecchio Frank 提出对于 UCAA，抗生素保守治疗的效果不逊于阑尾切除术，但对于伴有阑尾结石的 AA，首选手术治疗，因为这种情况会增加失败率及并发症发生率[33]。有相关研究表明，与手术治疗相比，抗生素治疗能显著降低并发症发生率。Similis 等人的 meta 分析显示，与立即阑尾切除术相比，保守治疗与整体并发症(伤口感染、腹部及盆腔脓肿、肠梗阻)明显较少相关[34]。在单用抗生素治疗 VS 手术切除治疗的成本分析中，Sippola S 等人的调查指出[35]手术组的总体社会成本是抗生素组的 1.6 倍。且与手术相比，成人患者接受抗生素治疗的病假时间较短。在不危及病人安全的情况下，努力缩短住院时间和缩短病假，将为社会节省大量生产力。另一项研究也表明使用口服抗生素，将大大缩短住院时间[36]。但同时，抗生素保守治疗有一定的治疗失败率及复发率。Brandon A. McCutcheon 等对 3236 名非复杂性急性阑尾炎患者的抗生素治疗的长期回顾性观察[37]显示所有抗生素患者的治疗失败率在 5.0%~7.5%之间。复发率为 4.4%~5.9%，抗生素治疗后穿孔的风险约为 3%。有声明指出，抗生素治疗可以成功治疗一些希望避免手术并接 44 受高风险(高达 38%)复发的 UCAA 患者[38]。

近些年，有研究分析了抗生素保守治疗成功的因素。Tyler J. Loftus 等人对 81 例 UCAA 患者进行了回顾性队列分析[39]，提示抗生素保守治疗成功的独立预测因素包括入院前症状持续时间较长(>25 h)、较低的体温(<37.3℃)、较低的修正 Alvarado 评分(<4 分)和较小的阑尾直径(<13 毫米)、无粪石阻塞。另外，Haijanen Jussi 等对一项阑尾炎治疗的随机对照试验进行二次分析[40]表明计算机断层扫描(computed tomography, CT)显示阑尾直径大于或等于 15 毫米，入院时体温大于 38℃与抗生素治疗的原发性无反应性相关。故临床医师针对阑尾炎患者选择抗生素保守治疗前，应该对患者阑尾腔直径、体温、有无粪石阻塞等进行综合评估，以降低治疗失败率及复发率。

### 3.3. 内镜逆行阑尾炎治疗

受内镜逆行胰胆管造影术(ERCP)成功治疗急性胆管炎的启发，2012 年刘冰熔教授提出了一种名为内镜逆行阑尾炎治疗的微创方法。ERAT 的目的是清除阑尾管腔阻塞(即急性阑尾炎的主要原因)，包括引流脓液、粪石取出和必要时置入支架，这也有助于确认急性阑尾炎的诊断，从而避免了切除正常阑尾的可能，未来可能会成为诊断阑尾炎的金标准。ERAT 能立即缓解腹痛，明显缩短住院时间。在 33 例急性阑尾炎患者中 32 例(97%)得到了成功的治疗。就患者的花费成本而言，ERAT 与腹腔镜阑尾切除术相当，但高于单独的抗生素治疗(左氧氟沙星 + 甲硝唑，为期 3 天)。ERAT 结束后阑尾炎在临床中的实际复发率约 3% [41]。除了上述优点，Ding Wenjuan 等[42]发现相对于阑尾切除术后的患者，ERAT 组患者的胆囊收缩素水平下降最小，炎症因子升高幅度也最小，血管活性肠肽水平明显降低，这表明 ERAT 手术对身体的伤害及胃肠功能的负面影响较小。而 ERAT 中充分的引流可能是减少阑尾炎复发的有效手段[43]。但需要注意的是，ERAT 过程中固体粪石完全堵塞阑尾和支架置入穿孔会导致治疗失败[41]。

## 4. 总结与思考

随着国内外医学研究的深入、医疗技术不断发展，针对非复杂性急性阑尾炎的治疗越发多样化。从最初的阑尾炎手术切除到如今的微创甚至无创治疗，不变的宗旨是尽量在保证治疗成功率的同时减少并发症的发生，并降低复发率，提高患者生活质量。这也对临床医师的素质提出了更高的要求。

对于阑尾的保留与切除各有利弊，尚未形成统一的意见。目前没有单独的炎症标志物(如白细胞计数、



CRP, 或降钙素原等)能够以高特异性和敏感性识别阑尾炎[44]。而 CT 虽然在诊断急性阑尾炎方面有约 95% 的敏感性, 但区分非复杂性阑尾炎和复杂性阑尾炎的敏感性只有 64% 左右[45]。如何进一步提高 UCAA 诊断的敏感性, 如何根据患者病情调整治疗方案, 如何缩短患者住院时间和减少花费, 这一系列问题仍是临床医务工作者需要思考的方向, 同时也应当让患者充分了解现有的治疗方案及其利弊, 以便根据自身情况做出合适的决定, 并从治疗方案中获益。

## 参考文献

- [1] Livingston, E.H., Woodward, W.A., Sarosi, G.A. and Haley, R.W. (2007) Disconnect between Incidence of Nonperforated and Perforated Appendicitis: Implications for Pathophysiology and Management. *Annals of Surgery*, **245**, 886-892. <https://doi.org/10.1097/01.sla.0000256391.05233.aa>
- [2] Vons, C., Barry, C., Maitre, S., et al. (2011) Amoxicillin plus Clavulanic Acid versus Appendectomy for Treatment of Acute Uncomplicated Appendicitis: An Open-Label, Non-Inferiority, Randomised Controlled Trial. *The Lancet*, **377**, 1573-1579. [https://doi.org/10.1016/S0140-6736\(11\)60410-8](https://doi.org/10.1016/S0140-6736(11)60410-8)
- [3] Ceresoli, M., Pisano, M., Allievi, N., et al. (2019) Never Put Equipoise in Appendix! Final Results of ASAA (Antibiotics vs. Surgery for Uncomplicated Acute Appendicitis in Adults) Randomized Controlled Trial. *Updates in Surgery*, **71**, 381-387. <https://doi.org/10.1007/s13304-018-00614-z>
- [4] Salminen, P., Paajanen, H., Rautio, T., et al. (2015) Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. *JAMA*, **313**, 2340-2348. <https://doi.org/10.1001/jama.2015.6154>
- [5] Moris, D., Paulson, E.K. and Pappas, T.N. (2021) Diagnosis and Management of Acute Appendicitis in Adults: A Review. *JAMA*, **326**, 2299-2311. <https://doi.org/10.1001/jama.2021.20502>
- [6] Bhangu, A., Søreide, K., Di Saverio, S., Assarsson, J.H. and Drake, F.T. (2015) Acute Appendicitis: Modern Understanding of Pathogenesis, Diagnosis, and Management. *The Lancet*, **386**, 1278-1287. [https://doi.org/10.1016/S0140-6736\(15\)00275-5](https://doi.org/10.1016/S0140-6736(15)00275-5)
- [7] Myers, E., Kavanagh, D.O., Ghous, H., Evoy, D. and McDermott, E.W. (2010) The Impact of Evolving Management Strategies on Negative Appendectomy Rate. *Colorectal Disease: The Official Journal of the Association of Coloproctology of Great Britain and Ireland*, **12**, 817-821. <https://doi.org/10.1111/j.1463-1318.2009.01910.x>
- [8] Seethahal, S.A., Bolorunduro, O.B., Sookdeo, T.C., Oyeturji, T.A., et al. (2010) Negative Appendectomy: A 10-Year Review of a Nationally Representative Sample. *The American Journal of Surgery*, **201**, 433-437. <https://doi.org/10.1016/j.amjsurg.2010.10.009>
- [9] Lu, C., Liu, C., Fuh, J., et al. (2007) Irritable Bowel Syndrome and Negative Appendectomy: A Prospective Multivariable Investigation. *Gut*, **56**, 655-660. <https://doi.org/10.1136/gut.2006.112672>
- [10] Renteria, O., Shahid, Z. and Huerta, S. (2018) Outcomes of Appendectomy in Elderly Veteran Patients. *Surgery*, **164**, 460-465. <https://doi.org/10.1016/j.surg.2018.04.027>
- [11] Kwan, H.T.L. (2010) Re: If Not Appendicitis, Then What Else Can It Be? A Retrospective Review of 1492 Appendectomies. *Hong Kong Medical Journal*, **16**, 12-17.
- [12] Slim, C., Ahmad, S., Abdellatif, A., et al. (2014) Histopathological Findings in Appendectomy Specimens: A Study of 24,697 Cases. *International Journal of Colorectal Disease*, **29**, 1009-1012. <https://doi.org/10.1007/s00384-014-1934-7>
- [13] Masahata, K., Umemoto, E., Kayama, H., et al. (2014) Generation of Colonic IgA-Secreting Cells in the Caecal Patch. *Nature Communications*, **5**, Article No. 3704. <https://doi.org/10.1038/ncomms4704>
- [14] Randal, B.R., Barbas, A.S., Bush, E.L., et al. (2007) Biofilms in the Large Bowel Suggest an Apparent Function of the Human Vermiform Appendix. *Journal of Theoretical Biology*, **249**, 826-831. <https://doi.org/10.1016/j.jtbi.2007.08.032>
- [15] Meng, W., Cai, S.-R., Zhou, L., Dong, Q., Zheng, S. and Zhang, S.-Z. (2009) Performance Value of High Risk Factors in Colorectal Cancer Screening in China. *World Journal of Gastroenterology*, **15**, 6111-6116. <https://doi.org/10.3748/wjg.15.6111>
- [16] Andersson, R.E., Olaison, G., Tysk, C., et al. (2003) Appendectomy Is Followed by Increased Risk of Crohn's Disease. *Gastroenterology*, **124**, 40-46. <https://doi.org/10.1053/gast.2003.50021>
- [17] Jaschinski, T., Mosch, C., Eikermann, M. and Neugebauer, E.A.M. (2015) Laparoscopic versus Open Appendectomy in Patients with Suspected Appendicitis: A Systematic Review of Meta-Analyses of Randomised Controlled Trials. *BMC Gastroenterology*, **15**, Article No. 48. <https://doi.org/10.1186/s12876-015-0277-3>
- [18] Yu, M.-C., Feng, Y.-J., Wang, W., et al. (2017) Is Laparoscopic Appendectomy Feasible for Complicated Appendicitis?

- A Systematic Review and Meta-Analysis. *International Journal of Surgery*, **40**, 187-197. <https://doi.org/10.1016/j.ijsu.2017.03.022>
- [19] Nakhamiyayev, V., Galldin, L., Chiarello, M., Lumba, A. and Gorecki, P.J. (2010) Laparoscopic Appendectomy Is the Preferred Approach for Appendicitis: A Retrospective Review of Two Practice Patterns. *Surgical Endoscopy*, **24**, 859-864. <https://doi.org/10.1007/s00464-009-0678-x>
- [20] Di Saverio, S., Podda, M., De Simone, B., et al. (2020) Diagnosis and Treatment of Acute Appendicitis: 2020 Update of the WSES Jerusalem Guidelines. *World Journal of Emergency Surgery: WJES*, **15**, 27. <https://doi.org/10.1186/s13017-020-00306-3>
- [21] Xue, C.R., Lin, B.Q., Huang, Z.Y. and Chen, Z. (2015) Single-Incision Laparoscopic Appendectomy versus Conventional 3-Port Laparoscopic Appendectomy for Appendicitis: An Updated Meta-Analysis of Randomized Controlled Trials. *Surgery Today*, **45**, 1179-1186. <https://doi.org/10.1007/s00595-014-1094-y>
- [22] Carter, J.T., Kaplan, J.A., Nguyen, J.N., et al. (2014) A Prospective, Randomized Controlled Trial of Single-Incision Laparoscopic vs Conventional 3-Port Laparoscopic Appendectomy for Treatment of Acute Appendicitis. *Journal of the American College of Surgeons*, **218**, 950-959. <https://doi.org/10.1016/j.jamcollsurg.2013.12.052>
- [23] Wang, D.Y., Dong, T., Shao, Y., Gu, T.T., Xu, Y. and Jiang, Y. (2019) Laparoscopy versus Open Appendectomy for Elderly Patients, a Meta-Analysis and Systematic Review. *BMC Surgery*, **19**, Article No. 54. <https://doi.org/10.1186/s12893-019-0515-7>
- [24] Kang, B.M., Choi, S.I., Kim, B.-S. and Lee, S.-H. (2018) Single-Port Laparoscopic Surgery in Uncomplicated Acute Appendicitis: A Randomized Controlled Trial. *Surgical Endoscopy*, **32**, 3131-3137. <https://doi.org/10.1007/s00464-018-6028-0>
- [25] Swank, H.A., van Rossem, C.C., van Geloven, A.A.W., et al. (2014) Endostapler or Endoloops for Securing the Appendiceal Stump in Laparoscopic Appendectomy: A Retrospective Cohort Study. *Surgical Endoscopy*, **28**, 576-583. <https://doi.org/10.1007/s00464-013-3207-x>
- [26] van Rossem, C.C., van Geloven, A.A.W., Schreinemacher Marc, H.F. and Bemelman, W.A. (2017) Endoloops or Endostapler Use in Laparoscopic Appendectomy for Acute Uncomplicated and Complicated Appendicitis: No Difference in Infectious Complications. *Surgical Endoscopy*, **31**, 178-184. <https://doi.org/10.1007/s00464-016-4951-5>
- [27] Qian, D.H., He, Z.G., Hua, J. and Song, Z.S. (2015) Stump Invagination versus Simple Ligation in Open Appendectomy: A Systematic Review and Meta-Analysis. *International Surgery*, **100**, 1199-1206. <https://doi.org/10.9738/INTSURG-D-15-00074.1>
- [28] van Dijk, S.T., van Dijk, A.H., Dijkgraaf, M.G. and Boermeester, M.A. (2018) Meta-Analysis of In-Hospital Delay before Surgery as a Risk Factor for Complications in Patients with Acute Appendicitis. *The British Journal of Surgery*, **105**, 933-945. <https://doi.org/10.1002/bjs.10873>
- [29] 王海宽, 李世宽, 李元博, 刘静, 窦榕榕, 渠雪红. 成人急性阑尾炎脓液的细菌培养及药敏试验[J]. 青岛大学医学院学报, 2011, 47(3): 255-257.
- [30] Kalligeros, M. and Mylonakis, E. (2019) In Uncomplicated Acute Appendicitis, 61% of Patients Initially Treated with Antibiotics Had Not Had Appendectomy at 5 Years. *Annals of Internal Medicine*, **170**, JC10. <https://doi.org/10.7326/ACPJC-2019-170-2-010>
- [31] Salminen, P., Paaanen, H., Rautio, T., et al. (2015) Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. *JAMA*, **313**, 2340-2348. <https://doi.org/10.1001/jama.2015.6154>
- [32] Paulina, S., Risto, T., Hannu, P., et al. (2018) Five-Year Follow-Up of Antibiotic Therapy for Uncomplicated Acute Appendicitis in the APPAC Randomized Clinical Trial. *JAMA*, **320**, 1259-1265. <https://doi.org/10.1001/jama.2018.13201>
- [33] Lo Vecchio, F. (2021) A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis. *New England Journal of Medicine*, **384**, 879-881. <https://doi.org/10.1056/NEJMc2035865>
- [34] Simillis, C., Symeonides, P., Shorthouse, A.J. and Tekkis, P.P. (2009) A Meta-Analysis Comparing Conservative Treatment versus Acute Appendectomy for Complicated Appendicitis (Abscess or Phlegmon). *Surgery*, **147**, 818-829. <https://doi.org/10.1016/j.surg.2009.11.013>
- [35] Sippola, S., Grönroos, J., Tuominen, R., et al. (2017) Economic Evaluation of Antibiotic Therapy versus Appendectomy for the Treatment of Uncomplicated Acute Appendicitis from the APPAC Randomized Clinical Trial. *The British Journal of Surgery*, **104**, 1355-1361. <https://doi.org/10.1002/bjs.10575>
- [36] Di Saverio, S., Sibilio, A., Giorgini, E., et al. (2014) The NOTA Study (Non Operative Treatment for Acute Appendicitis): Prospective Study on the Efficacy and Safety of Antibiotics (Amoxicillin and Clavulanic Acid) for Treating Patients with Right Lower Quadrant Abdominal Pain and Long-Term Follow-Up of Conservatively Treated Suspected Appendicitis. *Annals of Surgery*, **260**, 109-117. <https://doi.org/10.1097/SLA.0000000000000560>

- 
- [37] McCutcheon, B.A., Chang, D.C., Marcus, L.P., *et al.* (2014) Long-Term Outcomes of Patients with Nonsurgically Managed Uncomplicated Appendicitis. *Journal of the American College of Surgeons*, **218**, 905-913. <https://doi.org/10.1016/j.jamcollsurg.2014.01.003>
- [38] Di Saverio, S., Birindelli, A., Kelly, M.D., *et al.* (2016) WSES Jerusalem Guidelines for Diagnosis and Treatment of Acute Appendicitis. *World Journal of Emergency Surgery: WJES*, **11**, 34. <https://doi.org/10.1186/s13017-016-0090-5>
- [39] Loftus, T.J., Brakenridge, S.C., Croft, C.A., *et al.* (2018) Successful Nonoperative Management of Uncomplicated Appendicitis: Predictors and Outcomes. *Journal of Surgical Research*, **222**, 212-218.e2. <https://doi.org/10.1016/j.jss.2017.10.006>
- [40] Jussi, H., Suvi, S., Eliisa, L., *et al.* (2021) Factors Associated with Primary Nonresponsiveness to Antibiotics in Adults with Uncomplicated Acute Appendicitis: A Prespecified Secondary Analysis of a Randomized Clinical Trial. *JAMA Surgery*, **156**, 1179-1181. <https://doi.org/10.1001/jamasurg.2021.5003>
- [41] Liu, B.-R., Ma, X., Feng, J., *et al.* (2015) Endoscopic Retrograde Appendicitis Therapy (ERAT): A Multicenter Retrospective Study in China. *Surgical Endoscopy*, **29**, 905-909. <https://doi.org/10.1007/s00464-014-3750-0>
- [42] Ding, W.J., Du, Z.Q. and Zhou, X.R. (2022) Endoscopic Retrograde Appendicitis Therapy for Management of Acute Appendicitis. *Surgical Endoscopy*, **36**, 2480-2487. <https://doi.org/10.1007/s00464-021-08533-8>
- [43] Yang, B.H., Kong, L.J., Saif, U., *et al.* (2022) Endoscopic Retrograde Appendicitis Therapy vs. Laparoscopic Appendectomy for Uncomplicated Acute Appendicitis. *Endoscopy*, **54**, 747-754. <https://doi.org/10.1055/a-1737-6381>
- [44] Yu, C.-W., Juan, L.-I., Wu, M.-H., Shen, C.-J., Wu, J.-Y. and Lee, C.-C. (2013) Systematic Review and Meta-Analysis of the Diagnostic Accuracy of Procalcitonin, C-Reactive Protein and White Blood Cell Count for Suspected Acute Appendicitis. *The British Journal of Surgery*, **100**, 322-329. <https://doi.org/10.1002/bjs.9008>
- [45] Sippola, S., Virtanen, J., Tammilehto, V., *et al.* (2020) The Accuracy of Low-Dose Computed Tomography Protocol in Patients with Suspected Acute Appendicitis: The OPTICAP Study. *Annals of Surgery*, **271**, 332-338. <https://doi.org/10.1097/SLA.0000000000002976>