

述评·消化外科进展

胃癌微创外科的研究与技术进展

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【摘要】 胃癌是世界范围内常见的恶性肿瘤之一,其发病率和死亡率均位于我国恶性肿瘤前列。自 1992 年 Kitano 等完成世界第 1 例腹腔镜胃癌根治术以来,腹腔镜技术得到快速发展。经过 30 余年的探索与实践,我国胃癌临床诊断与治疗亦取得长足进步。国内外大量临床研究均证实腹腔镜胃癌根治术具有不亚于传统开腹手术近远期疗效。腹腔镜胃癌根治术具有创伤性小、术后胃肠功能恢复快、术后疼痛轻、平均住院时间短等特点,逐步取代开腹手术,成为胃癌外科的主流手术方式。随着胃癌手术治疗理念持续更新,新兴微创技术不断涌现,其中机器人手术系统和吲哚菁绿示踪技术等,在胃癌手术中的应用与日俱增,使胃癌外科更加微创、精准,并提高胃周淋巴结清扫质量,国内胃癌外科技术进一步精进。笔者结合国内外相关研究,以胃癌微创外科技术为主题,回顾归纳近年来最新进展,旨在系统阐述胃癌外科的现状和未来展望。相信未来,我国的胃癌临床诊断与治疗必将更为规范化、微创化、精准化,必将开展更多高质量的多中心临床研究和进一步深化胃癌诊断与治疗规范。

【关键词】 胃肿瘤; 微创外科; 腹腔镜胃癌根治术; 机器人胃癌根治术; 吲哚菁绿示踪淋巴结清扫术; 保脾脾门淋巴结清扫术

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Progress of research and technical in minimally invasive surgery for gastric cancer

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【Abstract】 Gastric cancer is one of the most common malignant tumors in the world, and its incidence and mortality are among the top of malignant tumors in China. Since Kitano *et al* complete the first laparoscopic radical gastrectomy for gastric cancer in the world in 1992, the laparoscopic technology has developed rapidly. After more than 30 years of exploration and practice, the clinical diagnosis and treatment of gastric cancer in China has also made considerable progress. A large number of clinical studies at home and abroad have confirmed that laparoscopic radical gastrectomy is no less effective than traditional open surgery in the short and long term. Laparoscopic radical gastrectomy has the characteristics of less trauma, faster recovery of gastrointestinal function, less postoperative pain, and shorter average hospital stay. It has gradually replaced open surgery as the mainstream surgical method for gastric cancer. As the concept of surgical treatment for gastric cancer continues to update, emerging minimally invasive technologies continue to emerge, including robotic surgery systems and indocyanine green tracing technology, which are increasingly used in gastric cancer surgery, making gastric cancer surgery more minimally invasive and accurate, the quality of perigastric lymph node dissection and the domestic gastric cancer surgery technology further improving. Based on the relevant research at home and abroad, the authors review and summarize the latest progress in recent years with the topic of minimally invasive surgery for gastric cancer, aiming to systematically describe the current situation and future prospects of gastric cancer surgery. It is believed that in the future, the clinical diagnosis and treatment of gastric cancer in

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China will be more standardized, minimally invasive and accurate, more high-quality multicenter clinical research will be carry out and the diagnosis and treatment of gastric cancer will be further improved in China.

【Key words】 Stomach neoplasms; Minimally invasive surgery; Laparoscopic radical gastrectomy; Robot radical gastrectomy; Indocyanine green fluorescence-guided lymphadenectomy; Spleen-preserving splenic hilar lymphadenectomy

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亚洲是胃癌高发地区,而我国是全世界胃癌发病率和病死率最高的国家,每年新发胃癌患者人数占全世界的 43.9%,严重威胁我国居民生命健康^[1]。30 余年来,国内学者积极开展相关研究以期改善胃癌患者远期预后。伴随质疑与争论,腹腔镜微创技术逐渐取代开腹手术,在不断临床实践和国内外多项临床研究证据的支持下,腹腔镜微创技术已成为胃癌外科治疗的主要手术方式^[2]。目前,胃癌微创技术陆续出现了机器人胃癌手术和吲哚菁绿淋巴结显像等创新技术。笔者相信:这些新技术促使胃癌外科向更微创、更精准、更安全的方向发展。

一、腹腔镜辅助胃癌根治术的进展

外科手术治疗是可切除进展期胃癌的首选方案,也是早期胃癌除内镜下切除的首选治疗方式。2009 年,我国成立腹腔镜胃肠外科研究组(Chinese laparoscopic gastrointestinal surgery study group, CLASS), CLASS-01 研究由此诞生。该研究对比腹腔镜胃癌手术与传统开腹手术治疗进展期远端胃癌患者的手术安全性及肿瘤学疗效,术后短期结果显示:两组患者的术后并发症发生率相当(15.2% 比 12.9%, $P=0.285$)^[3]。其 3 年随访结果显示:两组患者的 3 年总生存率(83.1% 比 85.2%, $P=0.28$)和 3 年无病生存率(76.5% 比 77.8%)相似^[4]。2022 年,其 5 年随访结果显示:两者总生存率相似(72.6% 比 76.3%, $P=0.19$)^[5]。2020 年 CLASS-02 研究结果显示:由经验丰富的外科医师对临床 I 期胃癌患者行腹腔镜全胃切除术的安全性与开腹全胃切除术相当,为腹腔镜全胃切除术治疗早期胃癌的肿瘤安全性研究提供高级别循证医学证据^[6]。韩国腹腔镜胃肠外科研究组(Korean laparoscopic gastrointestinal surgery study group, KCLASS)和日本临床肿瘤学研究组(Japan clinical oncology group, JCOG)也开展了类似研究。其研究结果均显示:与开腹远端胃切除术(open distal gastrectomy, ODG)比较,腹腔镜远端胃切除术(laparoscopic distal gastrectomy, LADG)可安全治疗临床 I 期胃癌^[7-8]。远期疗效方面, KCLASS-01 研究结果显示: LADG 和 ODG 患者的 5 年总生存率和肿瘤特异性生存率相似^[9]。JCOG0912 研究结果显示: LADG 与

ODG 两者的无复发生存率相似^[10]。对于局部进展期胃癌, KCLASS-02 研究结果显示: LADG 联合 D₂ 淋巴结清扫术短期优势在于并发症发生率低、恢复速度快、术后疼痛轻等,而无复发生存时间与 ODG 相当^[11-12]。随后,我国季加孚教授将腹腔镜技术研究对象扩展至接受新辅助化疗后的胃癌人群, 1 项评价局部进展期胃癌患者接受新辅助化疗后行腹腔镜胃癌手术或 ODG 的 RCT, 结果显示:腹腔镜组患者术后并发症发生率更低,且术后辅助化疗依从性更好^[13]。这表明对接受新辅助化疗的胃癌患者施行腹腔镜手术同样安全、可行。外科手术方式由开放手术演变成微创手术的过程已历经 30 余年。这是国内外医学专家不断探索与积累的成果,使微创外科技术成为胃癌外科的首选治疗方式。

二、机器人胃癌根治术的进展

机器人胃癌根治术始见于 2003 年 Hashizume 和 Sugimachi^[14]报道。国内外学者在深化腹腔镜手术技巧的同时,陆续开展机器人相关胃癌手术,以探索新技术带来的便利。2017 年,笔者中心率先开展机器人与腹腔镜远端胃癌根治术临床疗效的 RCT, 短期结果显示:机器人远端胃癌根治术(robotic distal gastrectomy, RDG)总并发症发生率更低,炎症反应更轻,胃外淋巴结清扫数目更多,术后恢复更快,可以更早开始术后辅助化疗^[15]。该研究结果为 RDG 在胃癌患者中的应用提供了依据,远期肿瘤学疗效仍在进一步随访中。2021 年,笔者中心的 1 项前瞻性研究结果显示:对于复杂的全胃根治术,与传统腹腔镜手术方式比较,机器人手术系统可为术者提供更精确的手术操作环境,从而让患者达到更佳微创效果的同时提高淋巴结清扫质量^[16]。同年,国内余佩武教授联合其他医学中心,回顾性分析 5 402 例行腹腔镜或机器人胃癌根治术的患者资料,采用 1:1 倾向性匹配分析,结果显示:机器人组的总并发症发生率低于腹腔镜组(12.6% 比 15.2%, $P=0.023$),且术中出血量更少,淋巴结清扫数目更多,因此,由经验丰富的外科医师行机器人胃癌根治术安全、可行^[17]。同年 9 月,日本 Ojima 等^[18]发布 1 项关于机器人与腹腔镜胃癌根治术的

RCT,结果显示:机器人手术并没有降低术后腹腔感染发生率(该研究的主要终点),但同样证实短期结局不劣于腹腔镜手术。上述研究均表明机器人胃癌手术安全可行,而目前仍缺乏关于机器人胃癌根治术远期结果的前瞻性研究报道。此外,笔者中心牵头的CLASS-13研究是1项对比机器人和腹腔镜全胃根治术在进展期胃中上部癌临床疗效的多中心RCT,现处于患者招募阶段。《中国机器人胃癌手术指南》规范机器人胃癌手术各类操作,以供同道参考借鉴^[19]。

三、吲哚菁绿示踪淋巴结清扫术的进展

根治性淋巴结切除术可显著提高胃癌患者的长期生存率和肿瘤分期的准确性。清扫更多的淋巴结逐渐成为术者的追求目标^[20-21]。然而,现阶段术中常根据术者经验在裸眼下进行淋巴结清扫。由于胃周复杂的血管解剖及淋巴引流,在不增加术中并发症的同时,高效精准地清扫足够多的淋巴结对术者特别是初学者仍有较大挑战。随着腹腔镜技术的不断发展,胃癌外科医师不断探索如何运用腹腔镜引导方便、准确地进行实时淋巴结导航,进行系统、充分地淋巴结清扫。

吲哚菁绿近红外光成像具有良好的组织穿透性,在可见光下能够比其他染料更好地识别肥厚脂肪组织内的淋巴结,其作为一种新型外科导航技术,在乳腺癌、非小细胞肺癌、早期胃癌等肿瘤前哨淋巴结定位上取得肯定的效果^[22-25]。2009年,Tajima等^[26]提出吲哚菁绿荧光成像引导的前哨淋巴结定位可能有助于预测胃癌淋巴结转移状态,特别是针对cT1期胃癌患者。此外,吲哚菁绿对于胃肠吻合口血供也具有监测性能。然而全世界范围内仍缺乏高水平的大样本RCT评价吲哚菁绿引导下的腹腔镜胃癌D₂淋巴结清扫术安全性、有效性和可行性。对此,笔者中心开展吲哚菁绿示踪引导下腹腔镜胃癌淋巴结清扫术的安全性和有效性的临床研究(Fuges-012),结果证实:在行D₂淋巴结清扫术的患者中,吲哚菁绿示踪技术可以显著增加平均淋巴结清扫数目[49.6(15.0)枚比41.7(10.2)枚, $P<0.001$],降低淋巴结清扫不符合率(31.8%比57.4%, $P<0.001$),且不增加术后并发症发生率(15.5%比16.3%, $P=0.86$),为吲哚菁绿示踪技术在胃癌手术中的应用提供有价值的循证医学证据^[27]。该研究在《JAMA Surgery》发表,杂志同期配发国际外科学会主席Marco G. Patt教授的社评:“该研究富有价值,对于西方世界的外科医师而言至关重要,并建议吲哚菁绿的使用简单有效,应常规应用于胃癌手术中”。在证实吲

哚菁绿使用的有效性之后,针对吲哚菁绿注射的最佳方法(术前黏膜下注射或术中浆膜下注射),目前尚无定论。笔者中心针对该疑问开展了1项前瞻性RCT,研究结果显示:将患者分为黏膜下或浆膜下注射吲哚菁绿,2组患者术中清扫的平均淋巴结总数、淋巴结清扫不符合率、术后并发症发生率比较,差异均无统计学意义,但浆膜下注射具有更优的操作便利性和更低的患者负担^[28]。该研究的发表,为术中浆膜下注射吲哚菁绿提供依据,进一步推动吲哚菁绿示踪技术在胃癌微创外科的应用。尽管吲哚菁绿示踪技术可提高胃癌根治术中淋巴结的检出数目,但其是否能改善胃癌患者的远期预后仍无定论。目前Fuges-012研究远期随访数据已整理完毕,可能会带来令人鼓舞的消息。同时,笔者中心还牵头开展关于吲哚菁绿示踪技术在局部进展期胃癌腹腔镜淋巴结清扫术中临床疗效的前瞻性多中心RCT(CLASS-11),目前患者仍在入组中,希望日后能进一步为吲哚菁绿在胃癌手术中的应用推广提供更高级别证据。

四、腹腔镜保脾脾门淋巴结清扫术的进展

基于JCOG0110的研究结果,第5版日本胃癌治疗指南将脾门淋巴结从D₂淋巴结清扫范围中移除,仅推荐对肿瘤侵犯胃大弯的近端胃癌患者施行脾门淋巴结清扫术(D₂+No.10)^[29]。2021年中国临床肿瘤学会发布的胃癌诊疗指南中,对原发肿瘤长径>6 cm,肿瘤位于胃大弯侧,且术前分期为T3期或T4期的中上部胃癌,建议行脾门淋巴结清扫^[30]。脾门淋巴结清扫是近端胃癌淋巴结清扫术的重点和难点,既往研究结果显示:脾门淋巴结(No.10LN_s组)的转移率达8.8%~20.9%,并且No.10淋巴结转移阳性患者的预后差,被认为是影响患者预后的独立危险因素^[31-32]。1998年日本胃癌协会将联合脾脏切除的脾门淋巴结清扫术列为清扫脾门淋巴结的标准手术方式。随后的10余年时间,学者逐渐意识到脾脏具有调节抗肿瘤免疫及其他重要作用。同时,随着手术经验和手术技巧的不断提升,许多学者开始探索保脾脾门淋巴结清扫术的安全性及可行性。已有多项研究结果显示:联合脾切除的脾门淋巴结清扫与保脾的脾门淋巴结清扫比较,前者术后并发症发生率更高,但长期生存率无明显改善^[33-34]。然而,由于脾门位置深在、血管解剖变异多、周围结构复杂及术中暴露困难等原因,在开腹手术中,术者需要将脾、胰体尾充分游离并托出体外,才可进行彻底的脾门淋巴结清扫。该操作具有挑战性,而术后又易出现脾扭转、脾游离等并发

症,使保脾的脾门淋巴结清扫术难以常规开展。随着腹腔镜胃癌根治术的逐渐推广与应用,腹腔镜下操作视野的放大作用和超声刀良好的止血分离效果,使术中可以更清晰地辨认胃周相关筋膜、筋膜间隙、血管及其分支,可以轻松地全程显露脾血管及其各级分支,从而顺利、高效地完成精确的脾动脉旁及脾门淋巴结清扫。笔者中心针对清扫脾门淋巴结亦研究出一套行之有效的“黄氏三步法”腹腔镜保脾脾门淋巴结清扫术,程序化清扫步骤能够更高效且安全地进行保脾脾门淋巴结清扫,有望缩短初学者的学习曲线^[35]。同时,笔者中心于2016年发起1项前瞻性、多中心临床研究(CLASS-04),探讨局部进展期胃上部癌患者施行腹腔镜保脾脾门淋巴结清扫术的临床疗效。其研究结果显示:由经验丰富的外科医师施行腹腔镜全胃切除术联合保脾脾门淋巴结清扫术治疗局部进展期胃上部癌患者安全可行,具有可接受的长期疗效^[36]。发生脾门淋巴结转移的患者预后较差,容易复发^[37]。Kinoshita等^[38]的1项回顾性研究结果显示:对于局部进展期近端胃癌患者,腹腔镜保脾脾门淋巴结清扫组相较于联合脾脏切除组的No.10组淋巴结检出数目相近,且保脾组具有较高的5年总生存率(91.1%比51.0%, $P=0.024$)和相似的无复发生存率(77.6%比41.5%, $P=0.051$)。笔者中心开展了1项单中心前瞻性RCT(Fuges-002),旨在探讨腹腔镜保脾脾门淋巴结清扫术(D_2 +No.10组)与常规腹腔镜胃癌根治术(D_2 组)治疗非大弯侧局部进展期胃上部癌的近远期疗效,共随机入组536例患者,最终 D_2 +No.10组和 D_2 组各有263例。其研究结果显示:腹腔镜保脾脾门淋巴结清扫术虽然未能显著改善总体非大弯侧的进展期胃上部癌患者的3年无病生存率,但对于肿瘤位于后壁的进展期胃上部癌患者,该手术方式可以提高患者的远期生存^[39]。该研究为保脾脾门淋巴结清扫术适应证的扩展和应用提供高级别循证医学证据。相信未来对胃癌患者实施精准、个体化的 D_2 胃癌根治+保脾脾门淋巴结清扫术的治疗理念会逐渐得到国内外学者认可。

五、结语

随着时代变迁,科技发展,临床技术与科技创新协同进步,我国胃癌外科技术翻开新篇章。近年来,我国持续在国际上发出“中国声音”,为胃癌诊断与治疗带来新理念,为胃癌患者带来个体化、精准化治疗。笔者认为:现阶段研究者仍需砥砺前行,把人民健康放在第1位,以临床为基石,科研为魂,携手发展,共同谱写未来胃癌治疗的新篇章。

利益冲突 所有作者均声明不存在利益冲突

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