doi: 10.13241/j.cnki.pmb.2020.03.015

腹腔镜结肠癌根治术治疗老年局部进展期结肠癌的疗效和安全性及对患者免疫功能的影响*

韩 刚[1] 龚航军[1△] 曹 羽[1] 张 云[1] 张言言[1] 张 旭[1] 周利红[2]

（1 上海中医药大学附属曙光医院胃肠外科 上海 201203；2 上海中医药大学附属曙光医院肿瘤科 上海 201203）

摘要 目的：比较分析腹腔镜和开腹结肠癌根治术治疗老年局部进展期结肠癌的临床疗效和安全性及对患者免疫功能的影响。**方法：**根据随机数字表法，将64例老年局部进展期结肠癌患者随机分为腹腔镜组和开腹组，每组各32例，分别接受腹腔镜、开腹结肠癌根治术治疗。比较两组手术相关指标、手术前后免疫功能变化、术后近远期并发症的发生情况及预后。**结果：**与开腹组比较，腹腔镜组患者手术时间明显延长，而术中出血量、胃肠功能恢复时间则明显缩短(P<0.05)。两组淋巴结清扫数比较差异无统计学意义(P>0.05)。术后3个月，腹腔镜组$CD4^+$、$CD4^+/CD8^+$比值均明显高于开腹组(P<0.05)，且与术前比较差异均无统计学意义(P>0.05)。与开腹组比较，腹腔镜组患者术后切口感染的发生率明显降低(P<0.05)，两组其他近期并发症如吻合口瘘、吻合口出血，远期并发症如黏连性肠梗阻、切口疝的发生率比较差异均无统计学意义(P>0.05)。腹腔镜组与开腹组术后2年的局部复发率、1年和2年生存率比较差异均无统计学意义(P>0.05)。**结论：**腹腔镜手术和开腹手术治疗老年局部进展期结肠癌患者的临床疗效和预后相当，但腹腔镜手术对患者的免疫功能影响更小，且安全性更高。

关键词：腹腔镜结肠癌根治术；局部进展期；老年；免疫功能；并发症

中图分类号：R735.35 **文献标识码：**A **文章编号：**1673-6273(2020)03-475-04

Efficacy and Safety of Laparoscopic Radical Resection of Colon Cancer in the Treatment of Elderly Patients with Locally Advanced Colon Cancer and Its Effect on the Immune Function*

HAN Gang[1], GONG Hang-jun[1△], CAO Yu[1], ZHANG Yun[1], ZHANG Yan-yan[1], ZHANG Xu[1], ZHOU Li-hong[2]

(1 Department of Gastrointestinal Surgery, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China; 2 Oncology Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China)

ABSTRACT Objective: To analyze the effects and safety of laparoscopy and laparoscopic radical resection of colon cancer, and influence on immune function in elderly patients with locally advanced colon cancer. **Methods:** According to the random number table, 64 elderly patients with locally advanced colon cancer were divided into two groups. Laparoscopic radical resection (laparoscope group, n=32) and open radical resection (open group, n=32) were used respectively. The operative indexes, changes of immune function before and after operation, incidence of postoperative complications and prognosis were compared between two groups. **Results:** Compared with open group, the operation time in laparoscope group was significantly increased, while the intraoperative blood loss and recovery time of gastrointestinal function were significantly reduced (P<0.05). No significant difference was found in the number of lymph node dissection between the two groups (P>0.05). Three months after surgery, the $CD4^+$ and $CD4^+/CD8^+$ ratios in laparoscope group were significantly higher than those in control group, with no statistically significant difference from the preoperative level(P>0.05), and all the indicators of immune function were significantly higher than those in open group (P<0.05). Compared with open group, the incidence of postoperative incision infection was significantly reduced in laparoscope group (P<0.05), while the incidence of other short-term complications such as anastomotic fistula and anastomotic bleeding, and long-term complications such as adhesive intestinal obstruction and incisional hernia were not statistically difference between two groups(P>0.05). The local recurrence rate, 1-year survival rate and 2-year survival rate of laparoscope group and open group were not statistically different (P>0.05). **Conclusions:** The clinical efficacy and prognosis of laparoscopic surgery and laparotomy in the treatment of elderly patients with locally advanced colon cancer are similar, but laparoscopic surgery has less effect on the immune function and higher safety.

Key words: Laparoscopic radical resection of colon cancer; Locally advanced; Elderly; Immune function; Complications

Chinese Library Classification(CLC): R735.35 Document code: A

Article ID: 1673-6273(2020)03-475-04

* 基金项目：国家自然科学基金面上项目(81673784)

作者简介：韩刚(1970-)，男，副主任医师，主要从事胃肠肿瘤外科的研究，E-mail：hanhang883@126.com

△ 通讯作者：龚航军，E-mail：hanjang@126.com

(收稿日期：2019-05-30 接受日期：2019-06-23)

前言

结肠癌是一种恶性程度较高的恶性肿瘤，其发病率居我国所有恶性肿瘤的第四位，且近年来呈不断上升趋势。由于结肠癌的临床症状较为隐匿，约 10%的患者确诊时已存在局部进展，若不能及时得到有效治疗，将严重影响患者的预后[1-3]。手术切除仍是目前结肠癌最为有效的治疗手段，以开腹结肠癌根治术技术最为成熟，但该术式切口和创伤大，术后疼痛剧烈，且恢复时间长[4-6]。随着微创理念和技术的不断普及，腹腔镜下结肠癌根治术以其创伤小、恢复快等优势应用愈发广泛，但其对局部进展期结肠癌患者的根治性及安全性仍缺乏足够循证学依据[7,8]。本研究主要分析和比较了腹腔镜与开放结肠癌根治术治疗老年局部进展期结肠癌的临床疗效和安全性及对患者免疫功能的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月 -2016 年 12 月我院收治的拟行结肠癌根治术的老年局部进展期结肠癌患者 64 例。入组标准：① 顺利实施根治性切除手术，并经手术病理确诊；② 年龄 60~80 岁，为首次手术，且术前未接受过放化疗等治疗；③ 病理分期为 T3 期且固有肌层浸润深度≥ 5 mm，或 T4 期；④ 排除中转开腹、术前受免疫治疗或免疫功能障碍者，梗阻、穿孔、粘连或明确侵犯周围结构者，以及严重感染、心肝肾功能障碍者。其中，男 37 例，女 27 例，年龄 60~79 岁，平均(67.7± 4.2)岁。体质量 45.1~72.6 kg，平均 (58.1± 6.4)kg；TNM 临床分期：T3 期 33 例，T4 期 31 例。按照随机数字表法，将 64 例患者分为腹腔镜组(n=32)、开腹组(n=32)。两组患者的性别构成比、年龄、体质量、病理分期及病灶部位等一般资料比较差异均无统计学意义(P>0.05)。本研究遵从赫尔辛基宣言原则，患者或家属均签署知情同意书。

1.2 手术方法

所有患者术前给予常规治疗，包括营养支持、胃肠减压、调节酸碱平衡及常规肠道准备等，麻醉方式选择气管插管全麻。开腹组采用传统开腹结肠癌根治术，手术入路及手术方式参照常规方法。腹腔镜组采用腹腔镜结肠癌根治术，具体手术方法：在脐部上方 2~ 3cm 穿刺建立压力 12~15 mmHg 的人工气腹，选择右下腹麦氏点处置入 10 mm TROCAR 作为观察孔，结合病灶所处位置设置其他操作孔，常规腹腔探查，明确病灶的位置、病变范围、是否转移。按照全结肠系膜切除术的原则，切开结肠内侧腹膜，并从根部切断肠系膜下动脉后结扎，再切断肠系膜下静脉，锐性分离结肠固有系膜。于腹壁适当位置取 5~6 cm 切口，切除系膜血管根部肿瘤，并经切口将游离系膜及病变的肠段拖出腹腔后切除，结肠远端采用吻合器性肠段吻合术后返回腹腔。间断缝合腹膜及肠系膜，反复冲洗切口后关腹。术后常规放置引流管，并给予抗生素预防感染治疗，同时予以严密监护。

1.3 观察指标

1.3.1 疗效指标 记录两组患者手术时间、术中出血量、淋巴结清扫数、胃肠道功能恢复时间。

1.3.2 免疫功能指标 分别于手术前、手术后 3 个月抽取清晨肘静脉血 3 mL，置于肝素抗凝管。采用美国 BD Pharmingen 公司生产的 FACS Calibur 流式细胞仪检测外周血 T 淋巴细胞亚群，包括 $CD4^+$(%)、$CD8^+$(%)及 $CD4^+/CD8^+$ 比值。

1.3.3 术后并发症的发生情况 记录术后切口感染、吻合口瘘、吻合口出血等围术期并发症，以及黏连性肠梗阻、切口疝等术后 3 个月内远期并发症的发生率。

1.3.4 预后 所有患者术后均定期要求门诊或电话随访，随访时间为 2 年，观察两组术后局部复发、生存率。

1.4 统计学方法

采用 SPSS 18.0 统计软件包。符合正态分布的计量资料采用均数± 标准差($\bar{x}$± s)表示，组间比较采用独立样本 t 检验；计数资料采用例数或率表示，组间比较采用 x^2 检验，以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组患者手术情况的比较

与开腹组比较，腹腔镜组患者手术时间明显延长，而术中出血量、胃肠功能恢复时间则明显减少(P<0.05)。两组淋巴结清扫数比较差异无统计学意义(P>0.05)。见表 1。

表 1 两组患者手术情况比较($\bar{x}$± s)

Table 1 Comparison of the surgical conditions between the two groups($\bar{x}$± s)

Groups	N	Operation time(min)	Intraoperative blood loss(mL)	Number of nodal dissection(piece)	Time of gastrointestinal function recovery(d)
Laparoscope group	32	192.4± 21.1	103.7± 17.5	13.8± 3.2	2.6± 0.3
Laparotomy group	32	143.8± 15.4	155.4± 24.7	14.6± 3.5	3.4± 0.4
t		10.52	9.66	0.95	9.05
P		<0.001	<0.001	0.344	<0.001

2.2 两组患者手术前后免疫功能的比较

术前，两组 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 比值比较差异均无统计学意义(P>0.05)；术后 3 个月，腹腔镜组 $CD4^+$、$CD4^+/CD8^+$ 比值与术前比较差异均无统计学意义(P>0.05)，且均明显高于开腹组(P<0.05)。见表 2。

2.3 两组患者并发症发生情况的比较

与开腹组比较，腹腔镜组患者术后切口感染的发生率明显降低(P<0.05)，两组其他近期并发症如吻合口瘘、吻合口出血，远期并发症如黏连性肠梗阻、切口疝的发生率比较差异均无统计学意义(P>0.05)。见表 3。

表 2 两组患者手术前后免疫功能的比较($\bar{x}\pm s$)

Table 2 Comparison of the immune function before and after surgery between the two groups($\bar{x}\pm s$)

Groups	$CD4^+$(%)		$CD8^+$(%)		$CD4^+/CD8^+$	
	Before operation	At 3 months after operation	Before operation	At 3 months after operation	Before operation	At 3 months after operation
Laparoscope group (n=32)	45.14± 6.23	44.64± 6.31	38.83± 4.69	34.12± 4.33*	1.39± 0.48	1.33± 0.25
Laparotomy group (n=32)	46.93± 5.19	40.14± 5.92*	37.16± 5.16	30.53± 4.64*	1.44± 0.52	1.21± 0.18*
t	1.25	2.94	1.35	3.20	0.40	2.20
P	0.216	0.005	0.180	0.002	0.691	0.031

Note: Compared with before operation, *P<0.05.

表 3 两组患者术后近远期并发症发生情况的比较[例(%)]

Table 3 Comparison of the incidence of postoperative complications between the two groups [n(%)]

Groups	N	Short-term complication			Long-term complication	
		Incision infection	Anastomotic fistula	Anastomotic bleeding	Incision hernial	Adhesion ileus
Laparoscope group	32	0(0)	6(18.8)	4(12.5)	1(3.3)	2(6.7)
Laparotomy group	32	5(15.6)	4(12.5)	5(15.6)	3(10.0)	5(16.7)
x^2		5.42	0.47	0.13	1.07	1.44
P		0.020	0.491	0.719	0.302	0.230

2.4 两组远期预后的比较

对患者随访 2 年,腹腔镜组与开腹组在术后局部复发率、1 年和 2 年生存率比较差异均无统计学意义(P>0.05)。见表 4。

表 4 两组远期预后比较[例(%)]

Table 4 Comparison of the long-term prognosis between the two groups [n(%)]

Groups	N	Local recurrence	1-year survival	2-year survival
Laparoscope group	32	17(53.1)	23(71.9)	18(56.3)
Laparotomy group	32	14(43.8)	26(81.3)	20(62.5)
x^2		0.56	0.78	0.26
P		0.453	0.376	0.611

3 讨论

手术切除是局部进展期结肠癌患者的首选治疗方法,但术后易复发、远处转移率高,预后往往较差[9,10]。研究显示 30%~40%的进展期结肠癌根治术患者术后可复发, 好发于术后 0.5~2 年,是影响生存率的最重要原因[11,12]。术后局部复发多见于肿瘤病灶的剥离面、邻近器官及局部淋巴结,其原因多与术中未能完全切除肉眼难以察觉的微小癌灶有关[13,14]。腹腔镜下结肠癌根治术短期疗效和安全性具有一定优势,但由于此类患者肠黏膜屏障受损严重,肿瘤细胞菌易扩散转移,该术式是否适用于局部进展期结肠癌患者,尤其远期临床疗效及预后是否更有优势尚存在一定争议[15]。

随着腹腔镜技术不断改进和发展,其在临床治疗适应症范围也不断扩大,且疗效与开腹手术愈发接近[16,17]。本研究结果显示腹腔镜组患者手术时间虽有所增加,但术中出血量少、胃肠功能恢复时间短,说明腹腔镜手术对老年局部进展期结肠癌的可行性和临床疗效。由于腹腔镜手术对术者要求更高,尤其是小肠、子宫等邻近脏器可能干扰镜下操作,造成手术时间有所延长,但随着手术病例的增加及操作熟练程度的提升,手术时间将进一步缩短[18]。淋巴结转移直接影响结肠癌的预后,故术中淋巴结的清扫数量与远期生存密切相关[19-21]。本组研究结果显示腹腔镜与开腹手术在淋巴结清扫方面具有相当的效果,甚至有研究认为腹腔镜下淋巴结清扫更为彻底,原因在于腹腔镜的视觉放大作用可使手术路径清晰,有利于术者解剖分离的精准度和获得足够的肿瘤切缘[22]。

细胞免疫是抗肿瘤免疫的主要形式,T 淋巴细胞亚群作为主要的免疫因子,在调节免疫功能方面具有重要作用,恶性肿瘤进展期 T 细胞亚群均存在不同程度紊乱。本研究结果显示腹腔镜和开腹手术均会影响患者免疫能力,但腹腔镜手术由于创伤小故免疫损伤能力小,可促进术后快速恢复[23,24],与王建辉等[25]研究结果一致。有研究显示老年进展期结肠癌患者术后 1 d 免疫力有所下降。术后 3 d 起因肿瘤负荷减小,对机体免疫

功能的抑制作用下降，T 淋巴细胞及免疫功能逐渐恢复，而腹腔镜手术的恢复速度更快[26,27]。此外，腹腔镜组的切口感染率明显下降，而两组吻合口瘘、吻合口出血、黏连性肠梗阻、切口疝等近远期并发症以及术后 2 年局部复发、生存率均无明显差异，再次验证腹腔镜手术可实现与传统开腹手术相似的根治效果。NCCN 指南并未将腹腔镜手术作为局部进展期结肠癌的最高级别推荐，且对于梗阻、穿孔、粘连或明确侵犯周围结构的高危患者，腹腔镜结肠癌手术仍不作推荐[28-30]。

综上所述，只要严格把握适应症，采用腹腔镜手术治疗老年局部进展期结肠癌患者同样可达到与开腹手术同样的临床疗效，且安全性更高，有利于患者术后免疫功能恢复。但本研究病例数有限，且随访时间尚短，其远期预后有待积累样本进一步研究。

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