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腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术对进展期胃癌患者肠黏膜屏障功能和腹腔微转移的影响 *

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摘要 目的:探讨腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术对进展期胃癌(AGC)患者肠黏膜屏障功能和腹腔微转移的影响。**方法:**选取 2016 年 12 月~2018 年 12 月我院收治的 105 例 AGC 患者,按随机数字表法分为对照组($n=52$)和实验组($n=53$),分别施行腹腔镜辅助胃癌 D2 根治术、腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术。观察两组手术情况(淋巴结清扫数量、手术时间、术中出血量、近切缘距离)、胃肠功能恢复指标(肛门排气时间、经口进食时间、肠鸣音恢复时间)、并发症、住院时间及术前、术后 1 d、3 d、7 d 肠黏膜屏障功能[尿乳果糖 / 甘露醇(L/M)、血清二胺氧化酶(DAO)]、气腹后、关腹前腹腔微转移指标[多巴胺脱羧酶(DDC)、癌胚抗原(CEA)],并于术后 12 个月随访两组复发率。**结果:**实验组术中出血量少于对照组($P<0.05$);两组经口进食时间、肛门排气时间、住院时间、肠鸣音恢复时间比较无差异($P>0.05$);术前、术后 1 d、3 d、7 d 两组血清 DAO 水平、尿 L/M 比较无差异($P>0.05$);关腹前实验组腹腔冲洗液 DDC、CEA 水平低于对照组($P<0.05$);两组并发症总发生率比较,差异无统计学意义($P>0.05$);术后 12 个月随访,实验组和对照组各失访 2 例,实验组复发率 3.92%(2/51)低于对照组 20.00%(10/50)($P<0.05$)。**结论:**腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术治疗 AGC,能有效降低术中出血量,恢复胃肠功能,减少腹腔微转移及术后复发,且未增加肠黏膜屏障功能损伤,安全性高。

关键词:腹腔镜辅助胃癌 D2 根治术;胃癌;进展期;复发率;胃肠功能;腹腔微转移;胃背侧系膜近胃端完整系膜切除术

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Effect of Laparoscopic Assisted D2 Radical Gastrectomy Combined with Complete Proximal Gastrectomy of Gastric Dorsal Mesentery on Intestinal Mucosal Barrier Function and Peritoneal Micrometastasis in Patients with Advanced Gastric Cancer*

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ABSTRACT Objective: To investigate the effect of laparoscopic assisted D2 radical gastrectomy combined with complete proximal gastrectomy of gastric dorsal mesentery on intestinal mucosal barrier function and peritoneal micrometastasis in patients with advanced gastric cancer (AGC). **Methods:** From December 2016 to December 2018, 105 patients with AGC in our hospital were selected. The patients were randomly divided into control group ($n=52$) and experimental group ($n=53$) by random number table method. Laparoscopic assisted D2 radical gastrectomy, laparoscopic assisted D2 radical gastrectomy combined with complete proximal gastrectomy of gastric dorsal mesentery were performed respectively. The operation conditions (number of lymph node dissection, operation time, intraoperative blood loss, distance to the resection margin), gastrointestinal function recovery index (anal exhaust time, oral feeding time, bowel sounds recovery time), complications, hospitalization time and before operation, 1 d, 3 d, 7 d after operation intestinal mucosal barrier function [urine lactulose / mannitol (L/M), serum diamine oxidase (DAO)], after pneumoperitoneum and before abdominal closure peritoneal micrometastasis indexes [dopamine decarboxylase (DDC), carcinoembryonic antigen (CEA)] were observed. The recurrence rates of the two groups were followed up 12 months after operation. **Results:** The intraoperative blood loss in experimental group was less than that in control group ($P<0.05$). There were no significant differences in the oral feeding time, anal exhaust time, bowel sounds recovery time and hospitalization time between the two groups ($P>0.05$). Before operation, 1 d, 3 d, 7 d after operation, there were no significant differences in serum DAO levels and urine L/M between two groups ($P>0.05$). The DDC and CEA levels in peritoneal lavage fluid in the ex-

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perimental group were lower than those in the control group before abdominal closure ($P<0.05$). There were no significant differences in the total incidence of complications between the two groups ($P>0.05$). 12 months after follow-up, 2 cases were lost in the experimental group and the control group. The recurrence rate of the experimental group was 3.92% (2/51) lower than that of the control group 20.00% (10/50) ($P<0.05$). **Conclusion:** Laparoscopic assisted D2 radical gastrectomy combined with complete proximal gastrectomy of gastric dorsal mesentery in the treatment of AGC can effectively reduce intraoperative blood loss, restore gastrointestinal function, reduce abdominal micrometastasis and postoperative recurrence, and does not increase intestinal mucosal barrier function damage, with high safety.

Key words: Laparoscopic assisted D2 radical gastrectomy; Gastric cancer; Advanced stage; Recurrence rate; Gastrointestinal function; Peritoneal micrometastasis; Complete proximal gastrectomy of gastric dorsal mesentery

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前言

胃癌为临床常见消化道恶性肿瘤,患者早期缺乏典型临床表现,其中90%确诊时已处于进展期^[1-3]。进展期胃癌(AGC)具有复发率高、预后差等特点,据统计数据显示,其5年生存率仅为54.4%^[4]。目前临床针对AGC主要采用手术治疗,其中腹腔镜辅助胃癌D2根治术最为常用,但并发症发生率较高。随着膜解剖理论发展,胃背侧系膜近胃端完整系膜切除术逐渐应用于临床,其主要是将淋巴结、癌转移灶的胃背侧系膜根部附着点完整切除,达到整块切除的目的,可最大程度预防胃系膜破裂、出血、误伤等,在缩短出血时间、减少术中出血量、彻底清扫淋巴结方面均有显著优势^[5-7]。此外,术中挤压、牵拉等操作会导致癌细胞脱落,种植于腹膜,造成腹腔微转移。多巴胺脱羧酶(DDC)、癌胚抗原(CEA)为敏感度较高的肿瘤标记物,通过检测腹腔冲洗液中DDC、CEA水平可有效判断腹腔游离癌细胞情况,评估腹腔微转移程度^[8-9],但DDC、CEA在腹腔镜辅助胃癌D2根治术联合胃背侧系膜近胃端完整系膜切除术围术期

变化如何,临床鲜少研究。基于此,本研究选取我院收治的AGC患者105例为研究对象,旨在侧重从肠黏膜屏障功能、腹腔微转移等方面分析腹腔镜辅助胃癌D2根治术联合胃背侧系膜近胃端完整系膜切除术的应用价值。现报告如下。

1 资料与方法

1.1 一般资料

选取2016年12月~2018年12月我院收治的105例AGC患者,纳入标准:均经病理检查确诊为胃癌;临床分期为II b~IIIb期;肿瘤直径<10 cm;患者或家属签署知情同意书。排除标准:合并腹腔播散或远处转移者;合并其他恶性肿瘤;心肝肾肺等重要脏器功能障碍者;胃出血;胃穿孔;上腹部手术史;术前行放化疗或免疫治疗者;凝血功能异常。按随机数字表法分为对照组(n=52)和实验组(n=53)。两组性别、年龄、体质质量指数(BMI)、肿瘤直径、临床分期、病理类型、肿瘤位置对比无统计学差异($P>0.05$),具有可比性。见表1。

表1 两组一般资料比较

Table 1 Comparison of general data between two groups

General data		Experimental group(n=53)	Control group(n=52)	χ^2/U	P
Gender	Male	32(60.38%)	32(61.54%)	0.015	0.903
	Female	21(39.62%)	20(38.46%)		
Age(years)		53.92± 5.86	54.63± 5.07	0.663	0.509
BMI(kg/m ²)		21.38± 2.03	22.01± 1.98	1.610	0.111
Tumor diameter (cm)	>5	18(33.96%)	15(28.85%)		
	3~5	25(47.17%)	26(50.00%)	0.502	0.616
	<3	10(18.87%)	11(21.15%)		
Tumor location	Gastric fundus	9(16.98%)	8(15.38%)		
	Gastric body	28(52.83%)	29(55.77%)	0.099	0.952
	Gastric antrum	16(30.19%)	15(28.85%)		
Clinical stages	II b	11(20.75%)	12(23.08%)		
	IIIa	24(45.28%)	25(48.08%)	0.496	0.620
	IIIb	18(33.96%)	15(28.85%)		
Pathological type	Well differentiated adenocarcinoma	6(11.32)	7(13.46%)	0.392	0.983
	Moderately well differentiated adenocarcinoma	14(26.42)	15(28.85%)		
	Moderately differentiated adenocarcinoma	22(41.51)	21(40.38%)		
	Poorly differentiated adenocarcinoma	8(15.09)	7(13.46%)		
	Signet ring cell carcinoma	3(5.66)	2(3.85%)		

1.2 治疗方法

两组术前均进行健康宣教,减轻焦虑,术前禁食5~6 h,术前2 h口服200 mL 5%的葡萄糖溶液,以减少饥饿感。对照组行腹腔镜辅助胃癌D2根治术:气管插管全麻,两腿分开平卧位,采用常规“5孔法”,于脐下缘作观察孔,建立压力为13 mmHg的CO₂气腹,探查腹腔,主操作孔为左侧腋前线肋缘下3 cm置入10 mm Trocar,牵引孔为左锁骨中线平脐上2 cm置入5 mm Trocar,右锁骨中线平脐上2 cm、右侧腋前线偏内侧肋下缘下3 cm分别置入5 mm Trocar为牵引孔。向头侧翻起大网膜,以超声刀于横结肠中部大网膜与附着处向左离断大网膜至结肠脾曲,右至结肠肝曲;胰尾部分分离出胃网膜左血管后以血管夹夹闭并离断,并将胃短血管和脾胃韧带离断;清扫胃网膜右血管淋巴结,肠系膜上静脉暴露,解剖胃结肠干,并清扫肠系膜上静脉淋巴结。分离胃网膜右动静脉,血管夹夹闭并离断,清扫No.6淋巴结。向头侧翻转胃窦,解剖胃十二指肠动脉,分离肝固有动脉、总动脉,清扫No.12淋巴结;分离胃右动静脉,对No.5淋巴结进行清扫;向头侧牵引胃,切除胰腺前被膜,分离胃左动静脉并切断;分离脾动脉,解剖血管周围淋巴结缔组织,向小弯侧剥离,清扫脾动脉近端淋巴结。采用超声刀对胃小弯进行裸化,清扫No.1、No.3淋巴结。于上腹部正中作切口(约5 cm)后以切口保护器保护,游离胃及大网膜并提出腹壁外,切除远端胃大部,行毕式消化道重建,冲洗术野,留置引流管,术毕。实验组行腹腔镜辅助胃癌D2根治术联合胃背侧系膜近胃端完整系膜切除术:取仰卧位,气管插管全麻联合硬脊膜外麻醉,寻找胃背侧系膜近胃端在横结肠系膜、肝总动脉、胰腺、门静脉、脾动脉等处附着点,将胃各系膜区域内脂肪组织、神经、淋巴结等清扫干净。行腹腔镜辅助胃癌D2根治术,手术体位、“5孔法”建立等操作同对照组,术中沿横结肠往大网膜游离,左至结肠脾曲,钝性分离横结肠系膜和胃网膜左系膜,显露胃网膜左系膜根部的胃网膜左血管,并采用超声刀离断。随后采用超声刀打开胃网膜右系膜与横结肠系膜三三交汇处的“膜桥”样结构,钝性分离,剥离胃网膜右系膜,清扫No.14v、No.6淋巴结。采用超声刀打开胰腺上缘循系膜附着,显露胃左动静脉、脾动脉、由脾动脉发出的胃后血管,以超声刀离断,胃左及胃后系膜进行完整分离后,清扫No.7、No.9、No.11淋巴结。显露胃右血管根部并离断,对No.5淋巴结进行清扫,显露固有动脉、肝门静脉,清扫No.12a淋巴结;沿肝总动脉向胃左血管系膜方向分离,清扫No.8a、No.8p淋巴结,与胃左血管系膜汇合,其余操作同对照组。两组术后均经硬脊膜外导管注入10 mL的0.125%布比卡因+2.5 mg/L芬太尼+生理盐水镇痛;静滴头孢呋辛1.5 g/次,间隔8 h一次,持续3~5 d,预防感染。术后24 h拔除

尿管,鼓励患者下床活动,术后3~4 d拔除引流管。均行SOX化疗,静滴奥沙利铂注射液(深圳海王药业有限公司,国药准字H20031048)130 mg/m²,d1,口服替吉奥胶囊(国药准字H20080802,山东新时代药业有限公司),体表面积>1.50 m²者40 mg/次,<1.25 m²者40 mg/次,1.25~1.50 m²者50 mg/次,d1~14,21 d为一个疗程,化疗≤6个疗程。

1.3 观察指标

(1)手术情况比较,包括手术时间、淋巴结清扫数量、术中出血量、近切缘距离。(2)两组胃肠功能恢复指标比较,包括肛门排气时间、经口进食时间、住院时间、肠鸣音恢复时间。(3)并发症发生率比较,包括肺部感染、胃瘫、切口感染、吻合口瘘等。(4)比较两组术前、术后1 d、3 d、7 d肠黏膜屏障功能,包括尿乳果糖/甘露醇(L/M)、血清二胺氧化酶(DAO)。检测方法:①术前晨起测试前将膀胱排空,50 mL乳果糖加甘露醇溶液(10 g乳果糖+5 g甘露醇)口服,口服测试液后6 h收集5 mL尿液,尿液冻存于-80°C待检;术后未能进食患者,晨起后排空留置导尿装置,经鼻肠管注入上述测试液,留取6 h尿液标本5 mL待检;采用高效液相色谱仪(美国赛默飞,UltiMate3000)以高效液相色谱法检测尿液L/M比值。②取晨空腹静脉血3 mL,室温凝固,以3500 r/min的转速、8 cm的半径离心10 min,分离取上层血清,置于-80°C恒温箱待测。采用北京中西远大科技有限公司提供的CN61M/721E型分光光度仪以活性比色法检测血清DAO水平,试剂盒购自上海远慕生物科技有限公司。(5)比较两组气腹后、关腹前腹腔微转移指标,包括癌胚抗原(CEA)、多巴胺脱羧酶(DDC)。检测方法:避开病灶位置,在腹腔注入无菌生理盐水250 mL,3 min后,抽吸冲洗液100 mL,离心分离,采用杭州诚信生物科技有限公司试剂盒和双抗体夹心酶联免疫吸附测定法测定。(6)术后12个月随访两组复发率。复发情况根据CT检查、胃镜活检组织病理、肿瘤标志物等综合结果判断。

1.4 统计学处理

采用SPSS22.0统计分析软件,以n(%)表示计数资料,两组间比较采用 χ^2 检验;计量资料以($\bar{x} \pm s$)表示,组内比较采用配对t检验,两组间比较采用独立样本t检验,等级资料采用秩和检验。检验水准为 $\alpha=0.05$ 。

2 结果

2.1 手术情况比较

实验组术中出血量少于对照组($P<0.05$),两组近切缘距离、淋巴结清扫数量、手术时间比较无显著差异($P>0.05$)。见表2。

表2 两组手术情况比较($\bar{x} \pm s$)

Table 2 Comparison of operation conditions between the two groups($\bar{x} \pm s$)

Groups	n	Number of lymph node dissection(n)	Operation time(min)	Intraoperative blood loss(mL)	Distance to the resection margin(cm)
Experimental group	53	28.05±5.33	150.11±15.53	60.13±12.15	5.46±0.58
Control group	52	26.51±7.12	146.12±16.47	105.91±20.49	5.51±0.54
t		1.256	1.277	13.957	0.457
P		0.212	0.205	<0.001	0.649

2.2 两组胃肠功能恢复指标、住院时间比较

两组肛门排气时间、经口进食时间、住院时间、肠鸣音恢复

时间比较无差异($P>0.05$)。见表3。

表3 两组胃肠功能恢复指标、住院时间比较($\bar{x}\pm s, d$)

Table 3 Comparison of gastrointestinal function recovery index and hospitalization time between the two groups ($\bar{x}\pm s, d$)

Groups	n	Oral feeding time	Anal exhaust time	Bowel sounds recovery time	Hospitalization time
Experimental group	53	3.01± 1.25	2.45± 0.73	3.62± 1.68	7.12± 1.85
Control group	52	3.18± 1.16	2.63± 0.61	3.51± 1.84	6.89± 1.72
t		0.722	1.370	0.321	0.660
P		0.472	0.174	0.748	0.511

2.3 两组肠黏膜屏障功能比较

术后1d、3d两组尿L/M、血清DAO水平均较术前显著升

高($P<0.05$)，术前、术后1d、3d、7d两组尿L/M、血清DAO水平比较，差异无统计学意义($P>0.05$)。见表4。

表4 两组肠黏膜屏障功能比较($\bar{x}\pm s$)

Table 4 Comparison of intestinal mucosal barrier function between the two groups ($\bar{x}\pm s$)

Groups	L/M				DAO(EU/mL)			
	Before operation	1 d after operation	3 d after operation	7 d after operation	Before operation	1 d after operation	3 d after operation	7 d after operation
Experimental group(n=53)	0.04± 0.02	0.32± 0.10*	0.27± 0.06*	0.10± 0.06	1.62± 0.35	3.92± 0.66*	3.30± 0.41*	1.90± 0.38
Control group(n=52)	0.04± 0.03	0.31± 0.12*	0.28± 0.06*	0.08± 0.05	1.65± 0.31	3.89± 0.72*	3.26± 0.53*	1.84± 0.40
t	0.000	0.464	0.854	1.854	0.465	0.223	0.433	0.788
P	1.000	0.644	0.395	0.067	0.643	0.824	0.666	0.432

Note: compared with before operation, * $P<0.05$.

2.4 两组腹腔微转移指标比较

气腹后两组腹腔冲洗液DDC、CEA水平比较，差异无统计

学意义($P>0.05$)，关腹前实验组腹腔冲洗液DDC、CEA水平低于对照组($P<0.05$)。见表5。

表5 两组腹腔微转移指标比较($\bar{x}\pm s, \text{ng/mL}$)

Table 5 Comparison of peritoneal micrometastasis indexes between the two groups ($\bar{x}\pm s, \text{ng/mL}$)

Groups	n	DDC		CEA	
		After pneumoperitoneum	Before abdominal closure	After pneumoperitoneum	Before abdominal closure
Experimental group	53	7.65± 2.14	65.31± 5.48	211.46± 23.35	738.38± 201.19
Control group	52	7.48± 2.36	78.27± 6.39	208.87± 25.12	1055.28± 235.25
t		0.387	11.163	0.548	7.423
P		0.700	<0.001	0.585	<0.001

3 讨论

胃癌D2根治术为既往临床治疗AGC的标准术式，手术操作以血管为导向，会导致周围组织过度牵拉^[10,11]，且相关数据显示，术后局部复发率高达38%~45%，严重影响患者预后恢复^[12]。随着胃癌手理念不断更新，“全胃系膜切除”逐渐应用于胃癌根治术，但术中常规切除胃及其血管、淋巴脂肪等组织并不可取，切除范围应为外科意义的胃系膜而非解剖学意义的胃系膜^[13-15]。因此，规范胃癌根治术切除范围，提高淋巴结清扫数

量，降低术后复发风险对患者预后改善具有重要意义。

腹腔镜辅助胃癌D2根治术联合胃背侧系膜近胃端完整系膜切除术是在“发丝样”疏松间隙内行手术操作，可避免损伤系膜及血管，减少组织的过度牵拉，降低术中出血量，缩短手术时间，同时有助于彻底清扫淋巴结^[16,17]。胃肠手术会导致炎性反应、肠道神经紊乱、肠道细菌移位等，改变内环境，影响术后胃肠功能恢复，而在胃系膜解剖边界进行操作的膜解剖理论，可使创伤减少，有利于胃肠功能恢复。党鹏远等^[18]研究证实，腹腔镜辅助胃癌D2根治术联合胃背侧系膜近胃端完整系膜切

除术治疗 AGC, 可减少术中出血量, 缩短手术时间, 清扫淋巴结更彻底, 促进恢复术后胃肠道功能, 促进患者及早恢复出院。本研究结果显示, 实验组术中出血量少于对照组, 与上述研究结果相似。传统的腹腔镜辅助胃癌 D2 根治术强调沿胃周血管进行淋巴结清扫, 但并不能界定脂肪结缔组织切除边界, 而系膜包绕胃及胃周围血管、周围脂肪结缔组织等, 形成独立空间, 其中可能存在直接侵犯、血行转移、腹膜播散、淋巴结扩散之外的第五转移, 而胃背侧系膜近胃端完整系膜切除术可沿此边界能够彻底清扫淋巴管网、系膜内淋巴结、可能的转移灶等, 进而提高淋巴结清扫数量。与上述研究不同的是, 本研究两组手术时间、肠鸣音恢复时间、住院时间、经口进食时间、肛门排气时间比较无差异, 这可能与术者操作经验、样本量小等因素有关。本研究还发现, 实验组并发症发生率仅为 7.55%, 安全性高。但相关研究发现, 术中胃系膜未完整切除、手术时间>240 min、术中出血量>160 mL 的 AGC 患者术后并发症发生风险较高^[19], 因此术中应遵循膜解剖理念, 保证胃系膜完整切除, 避免大范围清扫, 减少副损伤, 同时准确辨认胃背侧系膜各附着点, 在正确的膜间隙、层面内游离, 缩短手术时间, 并自根部完整切除胃背侧系膜在脾脏、胰腺、大血管表面附着点, 周围组织的牵拉减少, 降低系膜内小血管或淋巴结破裂出血风险, 减少手术并发症。

AGC 患者术后腹腔内可能残留微小病灶, 或由于手术操作导致癌细胞脱落并游离至腹膜, 成为术后腹膜转移或复发的病理基础^[20,21]。术后腹膜种植转移是导致胃癌复发的重要因素, 也是患者病死的主要原因, 相关报道指出, 胃癌术后病死患者中约 47.0%~50.0% 与腹膜种植转移及复发有关^[22]。本研究中关腹前实验组腹腔冲洗液 DDC、CEA 水平低于对照组, 术后 12 个月实验组复发率 3.92% 低于对照组 20.00% ($P < 0.05$)。DDC 可促进多巴胺代谢为多巴胺, 在多种恶性肿瘤疾病中异常高表达, 与细胞增殖、凋亡及血管生成密切相关^[23-25]。研究显示, 腹腔冲洗液中 DDC 水平与胃癌腹膜转移有关, 通过检测其水平变化可用于预测胃癌微转移风险^[26]。CEA 存在于上皮性肿瘤细胞内, 在胃肠道肿瘤诊断中具有较高的敏感性, 其腹腔冲洗液水平可反映胃癌腹膜转移及预后情况^[27]。腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术强调沿胃系膜解剖学边界行手术治疗, 能有效预防肿瘤复发或转移。上述结果表明, AGC 患者腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术后腹腔微转移风险更低, 这也是实验组复发率低的重要原因。

手术创伤、术中出血及机体应激反应会导致肠黏膜缺氧、缺血, 通透性增加, 致使肠黏膜屏障功能损伤。尿 L/M 可反映肠黏膜通透性, DAO 是一种肠黏膜上层绒毛膜细胞的细胞质内酶, 其血清水平可用于评估肠黏膜功能和结构完整性, 当肠黏膜受损时其水平异常升高。本研究中术后 1 d、3 d 两组尿 L/M、血清 DAO 水平均较术前升高, 但术后各时点组间对比无差异 ($P > 0.05$), 可见两种术式均会对患者肠黏膜屏障功能造成一定损伤, 但术后 7 d 逐渐恢复, 未产生远期影响。

综上可知, AGC 治疗采用腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术, 能有效降低术中出血量, 恢复胃肠功能, 减少腹腔微转移及术后复发, 且未增加肠黏膜屏障功能损伤, 安全性高。

参考文献(References)

- [1] Biagioli A, Skalamera I, Peri S, et al. Update on gastric cancer treatments and gene therapies [J]. Cancer Metastasis Rev, 2019, 38(3): 537-548
- [2] Shan C, Zhang Y, Hao X, et al. Biogenesis, functions and clinical significance of circRNAs in gastric cancer [J]. Mol Cancer, 2019, 18(1): 136
- [3] Kim SJ, Choi CW. Common Locations of Gastric Cancer: Review of Research from the Endoscopic Submucosal Dissection Era[J]. J Korean Med Sci, 2019, 34(35): e231
- [4] Lyons K, Le LC, Pham YT, et al. Gastric cancer: epidemiology, biology, and prevention: a mini review [J]. Eur J Cancer Pre, 2019, 28 (5): 397-412
- [5] van Boxel GI, Ruurda JP, van Hillegersberg R. Robotic-assisted gastrectomy for gastric cancer: a European perspective [J]. Gastric Cancer, 2019, 22(5): 909-919
- [6] Khan U, Shah MA. Ramucirumab for the treatment of gastric or gastro-esophageal junction cancer [J]. Expert Opin Biol Ther, 2019, 19 (11): 1135-1141
- [7] Pellino A, Riello E, Nappo F, et al. Targeted therapies in metastatic gastric cancer: Current knowledge and future perspectives[J]. World J Gastroenterol, 2019, 25(38): 5773-5788
- [8] 姬乐, 刘涛, 白浪, 等. 腹腔镜远端胃癌 D2 根治术对老年进展期胃癌病人 CEA、DDC 及血清 HIF-1 α 、MACCI 的影响[J]. 临床外科杂志, 2018, 26(10): 739-743
- [9] 王玉宏, 岳峰, 李明辉, 等. 胃癌浆膜受侵犯程度对根治术后腹腔转移风险的影响[J]. 现代中西医结合杂志, 2018, 27(27): 3024-3026
- [10] Beeharry MK, Zhu ZL, Liu WT, et al. Prophylactic HIPEC with radical D2 gastrectomy improves survival and peritoneal recurrence rates for locally advanced gastric cancer: personal experience from a randomized case control study[J]. BMC Cancer, 2019, 19(1): 932
- [11] 朱冠宇, 冯美燕, 李岩峰, 等. 腹腔镜与传统开腹胃癌 D2 根治术的临床分析[J]. 现代生物医学进展, 2017, 17(11): 2072-2075
- [12] Kanda M, Ito S, Mochizuki Y, et al. Multi-institutional analysis of the prognostic significance of postoperative complications after curative resection for gastric cancer[J]. Cancer Med, 2019, 8(11): 5194-5201
- [13] Xu ZY, Hu C, Chen S, et al. Evaluation of D2-plus radical resection for gastric cancer with pyloric invasion [J]. BMC Surg, 2019, 19(1): 172
- [14] Zhang J, Zou S, Luo R, et al. Is it worthy of adding dissection of the superior mesenteric vein lymph node (14v) to standard D2 gastrectomy for distal gastric cancers with No. 6 lymph node metastasis? [J]. Clin Transl Oncol, 2019, 21(12): 1699-170
- [15] 魏玉哲, 毕然, 王泽坤, 等. 腹腔镜下右站位 D2+ 全胃系膜切除远端胃癌根治术的操作技巧 [J]. 腹腔镜外科杂志, 2019, 24(3): 178-181
- [16] Beeharry MK, Zhu ZL, Liu WT, et al. Correction to: Prophylactic HIPEC with radical D2 gastrectomy improves survival and peritoneal recurrence rates for locally advanced gastric cancer: personal experience from a randomized case control study[J]. BMC Cancer, 2019, 19 (1): 1256
- [17] Purkayastha J, Yadav J, Talukdar A, et al. Radical Gastrectomy: Still the Gold Standard Treatment for Gastric Cancer-Our Experience from a Tertiary Care Center from Northeast India [J]. Indian J Surg Oncol, 2020, 11(1): 66-70
- [18] 党鹏远, 张淋, 张伟, 等. 腹腔镜辅助胃癌 D2 根治术联合胃背侧系膜近胃端完整系膜切除术治疗进展期胃癌的疗效[J]. 中华实用诊断与治疗杂志, 2020, 34(1): 20-23

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- [J]. ACS Applied Materials & Interfaces, 2019, 11(16): 14619-14629
- [15] Luo L, Zheng W, Lian G, et al. Combination treatment of adipose-derived stem cells and adiponectin attenuates pulmonary arterial hypertension in rats by inhibiting pulmonary arterial smooth muscle cell proliferation and regulating the AMPK/BMP/Smad pathway [J]. Int J Mol Med, 2018, 41(1): 51-60
- [16] Bacakova L, Zarubova J, Travnickova M, et al. Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells - a review [J]. Biotechnol Adv, 2018, 36(4): 1111-1126
- [17] Rohringer S, Hofbauer P, Schneider K, et al. Mechanisms of angiogenesis in 3D fibrin matrices mediated by the interaction of adipose-derived stem cells and endothelial cells [J]. Angiogenesis, 2014, 17(4): 921-933
- [18] Merfeldclauss S, Lupov I P, Lu H, et al. Adipose stromal cell contact with endothelial cells results in loss of complementary vasculogenic activity mediated by induction of activin[J]. Stem Cells, 2015, 33(10): 3039-3051
- [19] Kang H, Kang Y, Chun H J, et al. Evaluation of the in vitro and in vivo angiogenic effects of exendin-4 [J]. Biochemical and Biophysical Research Communications, 2013, 434(1): 150-154
- [20] Kang H, Sohn I, Jung J, et al. Exendin-4 protects hindlimb ischemic injury by inducing angiogenesis [J]. Biochem Biophys Res Commun, 2015, 465(4): 758-763
- [21] Bacci S, Laurino A, Manni M E, et al. The pro-healing effect of exendin-4 on wounds produced by abrasion in normoglycemic mice[J]. European Journal of Pharmacology, 2015, 764: 346-352
- [22] Lee J G, Ryu J H, Kim S M, et al. Replacement of the C-terminal Trp-cage of exendin-4 with a fatty acid improves therapeutic utility [J]. Biochemical Pharmacology, 2018, 151: 59-68
- [23] Holnthoner W, Hohenegger K, Husa A, et al. Adipose-derived stem cells induce vascular tube formation of outgrowth endothelial cells in a fibrin matrix [J]. Journal of Tissue Engineering and Regenerative Medicine, 2015, 9(2): 127-136
- [24] Goel H L, Mercurio A M. VEGF targets the tumour cell [J]. Nature Reviews Cancer, 2013, 13(12): 871-882
- [25] Andrae J, Gallini R, Betsholtz C, et al. Role of platelet-derived growth factors in physiology and medicine[J]. Genes & Development, 2008, 22(10): 1276-1312
- [26] Ruthenborg R J, Ban J J, Wazir A, et al. Regulation of wound healing and fibrosis by hypoxia and hypoxia-inducible factor-1[J]. Molecules and Cells, 2014, 37(9): 637-643
- [27] Zhang L, Luo X, Chen F, et al. LncRNA SNHG1 regulates cerebrovascular pathologies as a competing endogenous RNA through HIF-1 α /VEGF signaling in ischemic stroke [J]. Journal of Cellular Biochemistry, 2018, 119(7): 5460-5472
- [28] Liang H, Xiao J, Zhou Z, et al. Hypoxia induces miR-153 through the IRE1 α -XBP1 pathway to fine tune the HIF1 α /VEGFA axis in breast cancer angiogenesis[J]. Oncogene, 2018, 37(15): 1961-1975
- [29] Maybin J A, Murray A A, Saunders P T, et al. Hypoxia and hypoxia inducible factor-1 α are required for normal endometrial repair during menstruation[J]. Nature Communications, 2018, 9(1): 295
- [30] Nie C, Yang D, Xu J, et al. Locally administered adipose-derived stem cells accelerate wound healing through differentiation and vasculogenesis[J]. Cell Transplantation, 2011, 20(2): 205-216
- [31] Sun Z, Tong G, Kim T H, et al. PEGylated Exendin-4, a modified GLP-1 analog exhibits more potent cardioprotection than its unmodified parent molecule on a dose to dose basis in a murine model of myocardial infarction[J]. Theranostics, 2015, 5(3): 240-250

(上接第 3844 页)

- [19] 朱元增, 吴刚, 张建成, 等. 腹腔镜下胃背侧系膜完整切除 +D2 根治术治疗进展期胃癌的效果及术后并发症危险因素分析[J]. 中华实用诊断与治疗杂志, 2018, 32(6): 554-557
- [20] Li H, Xu CX, Gong RJ, et al. How does Helicobacter pylori cause gastric cancer through connexins: An opinion review[J]. World J Gastroenterol, 2019, 25(35): 5220-5232
- [21] Cainap C, Vlad C, Seicean A, et al. Gastric cancer: adjuvant chemotherapy versus chemoradiation. A clinical point of view [J]. J BUON, 2019, 24(6): 2209-221
- [22] 曾国祥, 黄文伟, 黄修仿. 腹腔镜辅助胃癌 D2 根治术的临床疗效及其对腹腔微转移的影响 [J]. 蚌埠医学院学报, 2018, 43(11): 1450-1452
- [23] Kim JH, Lee SY, Choi JE, et al. Polymorphism in ASCL1 target gene DDC is associated with clinical outcomes of small cell lung cancer patients[J]. Thorac Cancer, 2020, 11(1): 19-28
- [24] Shaikh MY, Burmeister J, Scott R, et al. Dosimetric evaluation of incorporating the revised V4.0 calibration protocol for breast intraoperative radiotherapy with the INTRABEAM system[J]. J Appl Clin Med Phys, 2020, 21(2): 50-59
- [25] 张慧, 陈景志, 陈建立, 等. DCC 和 MKK4 基因在结直肠癌组织中的表达及临床意义[J]. 陕西医学杂志, 2019, 48(8): 968-971
- [26] 肖毅频, 熊璐琪, 钟晓华, 等. 腹腔镜胃癌根治术对进展期胃癌患者腹腔冲洗液 CEA、DDC 浓度及炎性因子影响研究[J]. 临床和实验医学杂志, 2018, 17(9): 986-990
- [27] Nakanishi K, Kanda M, Umeda S, et al. The levels of SYT13 and CEA mRNAs in peritoneal lavages predict the peritoneal recurrence of gastric cancer[J]. Gastric Cancer, 2019, 22(6): 1143-1152