

·论著·

内镜黏膜下剥离术后行全腹腔镜远端胃切除术和直接行全腹腔镜远端胃切除术治疗早期胃癌的近期疗效

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【摘要】目的 探讨内镜黏膜下剥离术(ESD)后行全腹腔镜远端胃切除术(TLDG)和直接行TLDG治疗早期胃癌的近期疗效。**方法** 采用倾向评分匹配及回顾性队列研究方法。收集2014年3月至2019年12月南京医科大学第一附属医院收治的623例早期胃癌病人的临床病理资料;男405例,女218例;中位年龄为62岁,年龄范围为26~86岁。623例病人中,25例为ESD后行TLDG,设为ESD+TLDG组;598例为直接行TLDG,设为TLDG组。观察指标:(1)倾向评分匹配情况及匹配后两组病人一般资料比较。(2)TLDG术中和术后情况。(3)ESD+TLDG组病人分层分析。倾向评分匹配按1:2最近邻匹配法匹配。正态分布的计量资料以 $\bar{x}\pm s$ 表示,组间比较采用t检验。偏态分布的计量资料以M(范围)表示,组间比较采用Mann-Whitney U检验。计数资料以绝对数表示,组间比较采用 χ^2 检验或Fisher确切概率法。等级资料组间比较采用Mann-Whitney U检验。**结果** (1)倾向评分匹配情况及匹配后两组病人一般资料比较:623例病人中,75例配对成功,其中ESD+TLDG组25例,TLDG组50例。ESD+TLDG组病人倾向评分匹配前体质质量指数(BMI),肿瘤长径($\leq 20\text{ mm}$ 、 $21\sim 30\text{ mm}$ 、 $>30\text{ mm}$),临床分期(I期、II期、III期)分别为($22.3\pm 3.6\text{ kg/m}^2$,16、6、3例,24、1、0例,TLDG组病人上述指标分别为($24.3\pm 2.7\text{ kg/m}^2$,238、125、235例,312、126、160例,两组病人上述指标比较,差异均有统计学意义($t=2.744, Z=-2.834, -4.209, P<0.05$);经倾向评分匹配后两组病人BMI,肿瘤长径($\leq 20\text{ mm}$ 、 $21\sim 30\text{ mm}$ 、 $>30\text{ mm}$),临床分期(I期、II期)分别为($22.3\pm 3.6\text{ kg/m}^2$,16、6、3例,24、1例和($23.6\pm 2.9\text{ kg/m}^2$,29、12、9例,48、2例,两组病人上述指标比较,差异均无统计学意义($t=1.542, Z=-0.597, 0.000, P>0.05$)。(2)TLDG术中和术后情况:倾向评分匹配后两组病人TLDG手术时间、术后引流管拔除时间为180 min(124~289 min)、6 d(4~13 d)和170 min(106~250 min)、6 d(4~9 d),两组病人上述指标比较,差异均有统计学意义($Z=-2.396, -3.039, P<0.05$);两组病人术中出血量(<50 mL、50~100 mL,>100 mL),淋巴结清扫数目,术后住院时间,围术期并发症(切口脂肪液化、术后胃瘫、吻合口出血、肺部感染)分别为7、9、9例,34枚(16~58枚),8 d(6~31 d),1、1、0、0例和170 min(106~250 min),18、26、6例,39枚(22~68枚),8 d(6~29 d),0、0、1、1例,两组病人上述指标比较,差异均无统计学意义($Z=-1.703, -1.958, -1.139, \chi^2=0.033, P>0.05$)。发生吻合口出血病人经内镜下止血后缓解,其余并发症病人经保守治疗后均缓解。(3)ESD+TLDG组病人分层分析:①5例ESD后 ≤ 14 d行TLDG病人与20例ESD后 >14 d行TLDG病人,TLDG手术时间、术中出血量(<50 mL、50~100 mL,>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为200 min(170~289 min),0、3、2例,36枚(9~57枚),7 d(5~9 d),8 d(7~9 d),1例和180 min(124~253 min),8、6、6例,34枚(8~78枚),6 d(4~13 d),8 d(6~31 d),1例,TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=-1.536, -1.993, -0.238, -0.932, -0.589, P>0.05$),围术期并发

DOI: 10.3760/cma.j.cn115610-20210301-00104

收稿日期 2021-03-01

引用本文:李沣员,宣哲,徐皓,等.内镜黏膜下剥离术后行全腹腔镜远端胃切除术和直接行全腹腔镜远端胃切除术治疗早期胃癌的近期疗效[J].中华消化外科杂志,2021,20(5): 519~527. DOI: 10.3760/cma.j.cn115610-20210301-00104.



症比较,差异无统计学意义($P>0.05$)。②13例ESD后 ≤ 21 d行TLDG病人与12例ESD后 >21 d行TLDG病人,TLDG手术时间,术中出血量(<50 mL、50~100 mL、>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为200 min(145~289 min),2、6、5例,34枚(8~57枚),6 d(4~11 d),8 d(6~11 d),1例和179 min(124~240 min),6、3、3例,34枚(16~78枚),6 d(5~13 d),8 d(6~31 d),1例;TLDG手术时间比较,差异有统计学意义($Z=-2.241, P<0.05$),TLDG术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=-1.471, -0.163, -0.084, -0.194, P>0.05$),围术期并发症比较,差异无统计学意义($P>0.05$)。③15例ESD后 ≤ 28 d行TLDG病人与10例ESD后 >28 d行TLDG病人,TLDG手术时间,术中出血量(<50 mL、50~100 mL、>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为190 min(145~289 min),2、7、6例,33枚(8~57枚),6 d(4~11 d),8 d(6~31 d),1例和179 min(124~240 min),6、2、2例,37枚(16~78枚),6 d(5~13 d),8 d(6~14 d),1例,TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=-1.619, -2.000, -0.667, -0.370, -0.057, P>0.05$),围术期并发症比较,差异无统计学意义($P>0.05$)。结论 与直接行TLDG比较,早期胃癌行ESD+TLDG会延长TLDG手术时间和术后引流管拔除时间,但不影响近期疗效;早期胃癌ESD后 ≤ 21 d行TLDG与 >21 d行TLDG手术时间比较,差异有统计学意义。

【关键词】 胃肿瘤; 内镜黏膜下剥离术; 全腹腔镜远端胃切除术; 安全性; 近期疗效; 腹腔镜检查

基金项目:国家自然科学基金(81871946);江苏省重点研发计划(BE2016786);南京医科大学第一附属医院创新研究团队发展规划;江苏省高等学校重点学科建设项目(PAPD,JX10231801);江苏省重点医学学科(ZDXKA2016005);南京医科大学肿瘤个体化医学协同创新中心

Short-term efficacy of totally laparoscopic distal gastrectomy after endoscopic submucosal dissection versus totally laparoscopic distal gastrectomy for early gastric cancer

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[Abstract] **Objective** To investigate the short-term efficacy of totally laparoscopic distal gastrectomy (TLDG) after endoscopic submucosal dissection (ESD) versus direct TLDG for early gastric cancer. **Methods** The propensity score matching and retrospective cohort study was conducted. The clinicopathological data of 623 patients with early gastric cancer who were admitted to the First Affiliated Hospital of Nanjing Medical University from March 2014 to December 2019 were collected. There were 405 males and 218 females, aged from 26 to 86 years, with a median age of 62 years. Of 623 patients, 25 cases undergoing TLDG after ESD were divided into ESD+TLDG group and 598 cases undergoing TLDG directly were divided into TLDG group. Observation indicators: (1) the propensity score matching conditions and comparison of general data between the two groups after propensity score matching; (2) intraoperative and postoperative situations of TLDG; (3) stratification analysis of the ESD+TLDG group. The propensity score matching was conducted by 1: 2 matching using the nearest neighbor method. Measurement data with normal distribution were represented as $Mean \pm SD$, and comparison between groups was done using the t test. Measurement data with skewed distribution were represented as M (range) and comparison between groups was done using the Mann-Whitney U test. Count data were represented as absolute numbers, and comparison between groups was analyzed using the chi-square test or Fisher exact probability. Comparison of ordinal data between groups was analyzed using the Mann-Whitney U test. **Results** (1) The propensity score matching conditions and comparison of general data between the two groups after propensity score matching: 75 of 623 patients had successful matching, including 25 in the ESD+TLDG group and 50 in the TLDG group. Before propensity score matching, the body mass index (BMI), cases with tumor diameter ≤ 20 mm, 21 to 30 mm or >30 mm, cases with tumor classified as stage I, stage II or stage III of clinical staging were $(22.3 \pm 3.6) \text{ kg/m}^2$, 16, 6, 3, 24, 1, 0 of the ESD+TLDG group, respectively, versus $(24.3 \pm 2.7) \text{ kg/m}^2$, 238, 125, 235, 312, 126, 160 of the TLDG group, showing significant differences in the above indicators between the

two groups ($t=2.744$, $Z=-2.834$, -4.209 , $P<0.05$). After propensity score matching, the BMI, cases with tumor diameter ≤ 20 mm, 21 to 30 mm or >30 mm, cases with tumor classified as stage I or stage II of clinical staging were $(22.3\pm3.6)\text{kg}/\text{m}^2$, 16, 6, 3, 24, 1 of the ESD+TLDG group, versus $(23.6\pm2.9)\text{kg}/\text{m}^2$, 29, 12, 9, 48, 2 of the TLDG group, showing no significant difference between the two groups ($t=1.542$, $Z=-0.597$, 0.000, $P>0.05$). (2) Intraoperative and postoperative situations of TLDG: after propensity score matching, the operation time and time to postoperative drainage tube removal were 180 minutes(range, 124 to 289 minutes) and 6 days(range, 4 to 13 days) of the ESD+TLDG group, respectively, versus 170 minutes(range, 106 to 250 minutes) and 6 days (range, 4 to 9 days) of the TLDG group, showing significant differences between the two groups ($Z=-2.396$, -3.039 , $P<0.05$). Cases with the volume of intraoperative blood loss <50 mL, 50 to 100 mL or >100 mL, the number of lymph node dissected, duration of postoperative hospital stay, cases with perioperative complications as incision fat liquefaction, delayed gastric emptying, anastomotic bleeding or pulmonary infection were 7, 9, 9, 34(range, 16 to 58), 8 days(range, 6 to 31 days), 1, 1, 0, 0 of the ESD+TLDG group, respectively, versus 18, 26, 6, 39 (range, 22 to 68), 8 days (range, 6 to 29 days), 0, 0, 1, 1 of the TLDG group, showing no significant difference between the two groups ($Z=-1.703$, -1.958 , -1.139 , $\chi^2=0.033$, $P>0.05$). Cases with anastomotic bleeding were recovered after hemostasis under endoscopy and cases with other perioperative complications were recovered after conservative treatment. (3) Stratification analysis of the ESD+TLDG group. ① For 5 cases undergoing TLDG ≤ 14 days after ESD and 20 cases undergoing TLDG >14 days after ESD, the operation time of TLDG, cases with the volume of intraoperative blood loss <50 mL, 50 to 100 mL or >100 mL during TLDG, the number of lymph node dissected, time to postoperative drainage tube removal, duration of postoperative hospital stay, cases with perioperative complications were 200 minutes(range, 170 to 289 minutes), 0, 3, 2, 36(range, 9 to 57), 7 days(range, 5 to 9 days), 8 days(range, 7 to 9 days), 1 and 180 minutes (range, 124 to 253 minutes), 8, 6, 6, 34(range, 8 to 78), 6 days(range, 4 to 13 days), 8 days(range, 6 to 31 days), 1, respectively, showing no significant difference in the operation time of TLDG, volume of intraoperative blood loss during TLDG, the number of lymph node dissected, time to postoperative tube removal and duration of postoperative hospital stay between the two groups ($Z=-1.536$, -1.993 , -0.238 , -0.932 , -0.589 , $P>0.05$), and no significant difference in cases with perioperative complications between the two groups ($P>0.05$). ② For 13 cases undergoing TLDG ≤ 21 days after ESD and cases undergoing TLDG >21 days after ESD, the operation time of TLDG, cases with the volume of intraoperative blood loss as <50 mL, 50 to 100 mL or >100 mL during TLDG, the number of lymph node dissected, time to postoperative drainage tube removal, duration of postoperative hospital stay, cases with perioperative complications were 200 minutes(range, 145 to 289 minutes), 2, 6, 5, 34(range, 8 to 57), 6 days(range, 4 to 11 days), 8 days(range, 6 to 11 days), 1 and 179 minutes(range, 124 to 240 minutes), 6, 3, 3, 34(range, 16 to 78), 6 days(range, 5 to 13 days), 8 days(range, 6 to 31 days), 1, respectively, showing a significant difference in the operation time of TLDG between the two groups ($Z=-2.241$, $P<0.05$), while showing no significant difference in the volume of intraoperative blood loss during TLDG, the number of lymph node dissected, time to postoperative drainage tube removal, duration of postoperative hospital stay between the two groups ($Z=-1.471$, -0.163 , -0.084 , -0.194 , $P>0.05$) and no significant difference in cases with perioperative complications between the two groups ($P>0.05$). ③ For 15 cases undergoing TLDG ≤ 28 days after ESD and 10 cases undergoing TLDG >28 days after ESD, the operation time of TLDG, cases with the volume of intraoperative blood loss <50 mL, 50 to 100 mL or >100 mL during TLDG, the number of lymph node dissected, time to postoperative drainage tube removal, duration of postoperative hospital stay, cases with perioperative complications were 190 minutes (range, 145 to 289 minutes), 2, 7, 6, 33(range, 8 to 57), 6 days(range, 4 to 11 days), 8 days(range, 6 to 31 days), 1 and 179 minutes(range, 124 to 240 minutes), 6, 2, 2, 37(range, 16 to 78), 6 days (range, 5 to 13 days), 8 days(range, 6 to 14 days), 1, respectively, showing no significant difference in the operation time of TLDG, volume of intraoperative blood loss during TLDG, the number of lymph node dissected, time to postoperative tube removal and duration of postoperative hospital stay between the two groups ($Z=-1.619$, -2.000 , -0.667 , -0.370 , -0.057 , $P>0.05$), and no significant difference in cases with perioperative complications between the two groups ($P>0.05$). **Conclusions** Compared with cases undergoing TLDG directly, the operation time to TLDG and time to drainage tube removal after TLDG for cases undergoing ESD+TLDG are prolonged, but there is no difference in the short-term efficacy. For cases undergoing TLDG ≤ 21 days after ESD and cases undergoing TLDG >21 days after ESD, there is a significant difference in the operation time of TLDG.

[Key words] Gastric neoplasms; Endoscopic submucosal dissection; Totally laparoscopic distal gastrectomy; Safety; Short-term efficacy; Laparoscopy

Fund programs: National Natural Science Foundation of China (81871946); Primary Research & Development Plan of Jiangsu Province (BE2016786); Program for Development of Innovative Research Team in the First Affiliated Hospital of NJMU; Priority Academic Program Development of Jiangsu Provincial Higher Education Institutions (PAPD, JX10231801); Jiangsu Provincial Key Medical Discipline (ZDXKA2016005); Collaborative Innovation Center for Cancer Personalized Medicine of Nanjing Medical University

胃癌是全世界第五大常见恶性肿瘤,也是肿瘤致死的第三大原因^[1]。早期胃癌为病灶仅限于黏膜或黏膜下层,而无论肿瘤长径或淋巴结转移^[2]。内镜黏膜下剥离术(endoscopic submucosal dissection, ESD)作为早期胃癌的一种治疗方法,由于其具有术后病人恢复快、痛苦少等优点,获得广泛应用,适应证也逐渐扩大。但是,ESD的应用也促使非治愈性切除的早期胃癌病人逐渐增加,对于这部分病人应采取合适后续治疗^[3-5]。ESD可导致胃壁及其周围组织炎症反应,部分病人行ESD时,肿瘤部位穿孔会引起术后周围组织粘连,增加后续行腹腔镜手术难度和升高术后并发症发生率^[6-7]。目前,针对早期胃癌ESD后行腹腔镜远端胃切除术的临床研究较少^[8]。本研究回顾性分析2014年3月至2019年12月我中心收治的623例早期胃癌病人的临床病理资料,探讨ESD后行全腹腔镜远端胃切除术(totally laparoscopic distal gastrectomy, TLDG)和直接行TLDG治疗早期胃癌的近期疗效。

资料与方法

一、一般资料

采用倾向评分匹配及回顾性队列研究方法。收集623例早期胃癌病人的临床病理资料;男405例,女218例;中位年龄为62岁,年龄范围为26~86岁。623例病人中,25例为ESD后行TLDG,设为ESD+TLDG组;598例为直接行TLDG,设为TLDG组。两组病人BMI、肿瘤长径、临床分期比较,差异均有统计学意义($P<0.05$),性别、年龄、肿瘤位置、术前合并症比较,差异均无统计学意义($P>0.05$)。见表1。本研究通过我院医学伦理委员会审批,批号为2015-SR-081。病人及家属均签署知情同意书。

二、纳入标准和排除标准

纳入标准:(1)组织病理学检查结果为胃腺癌且无远处转移。(2)既往无胃外科手术及内镜手术史。(3)ESD未满足治愈性切除^[2]。(4)行TLDG。(5)临床病理资料完整。

排除标准:(1)妊娠或哺乳期。(2)5年内罹患

表1 ESD+TLDG组和TLDG组早期胃癌病人倾向评分匹配前一般资料比较

Table 1 Comparison of general data of early gastric cancer patients between totally laparoscopic distal gastrectomy after endoscopic submucosal dissection group and totally laparoscopic distal gastrectomy group

组别	例数	before propensity score matching								
		性别(例)		年龄 ($\bar{x}\pm s$,岁)	体质质量指数 ($\bar{x}\pm s$,kg/m ²)	肿瘤位置(例)		肿瘤长径(例)		
		男	女			胃中部	胃下部	≤20 mm	21~30 mm	>30 mm
ESD+TLDG组	25	17	8	59±11	22.3±3.6	9	16	16	6	3
TLDG组	598	388	210	61±11	24.3±2.7	189	409	238	125	235
统计值		$\chi^2=0.103$	$t=0.914$		$t=2.744$		$\chi^2=0.214$		$Z=-2.834$	
P值		>0.05	>0.05		<0.05		>0.05		<0.05	
组别	临床分期(例)								术前合并症(例)	
	I期	II期	III期		高血压病	冠心病	2型糖尿病	其他		
ESD+TLDG组	25	24	1	0	8	1	4	3		
TLDG组	598	312	126	160	159	31	123	82		
统计值				$Z=-4.209$			$\chi^2=0.045$			
P值				<0.05			>0.05			

注:ESD+TLDG组早期胃癌病人行内镜黏膜下剥离术+全腹腔镜远端胃切除术,TLDG组早期胃癌病人行全腹腔镜远端胃切除术

其他恶性肿瘤。(3)术前体温 $\geq 38^{\circ}\text{C}$ 或并发需要系统治疗的感染性疾病。(4)严重精神疾病、呼吸系统疾病或肝肾功能不全。(5)6个月内有不稳定心绞痛史或心肌梗死病史,6个月内脑梗死或脑出血病史,1个月内持续性应用糖皮质激素治疗(局部应用除外)。(6)临床病理资料缺失。

三、手术治疗

(一) ESD

手术操作参照文献[2],均由南京医科大学第一附属医院消化内科或内镜中心完成;病人经术后组织病理学检查确认未满足治愈性切除,于ESD后4个月内行TLDG。

(二) TLDG

手术操作参照文献[2],均由我科高年资医师完成。

四、观察指标和评价标准

观察指标:(1)倾向评分匹配情况及匹配后两组病人一般资料比较:采用倾向评分匹配法对两组病人资料进行匹配,消除BMI、肿瘤长径、临床分期因素混杂偏倚。匹配后比较两组病人性别、年龄、BMI、肿瘤位置、肿瘤长径、临床分期、术前合并症。(2)TLDG术中和术后情况:比较倾向评分匹配后两组病人TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间、围术期并发症。(3)ESD+TLDG组病人分层分析:ESD+TLDG组病人ESD后不同时间间隔行TLDG术中和术后情况,包括TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间、

围术期并发症。

评价标准:TLDG后并发症根据Clavien-Dindo外科手术并发症分级^[9]。

五、统计学分析

应用SPSS 18.0统计软件进行分析。倾向评分匹配按1:2最近邻匹配法匹配。正态分布的计量资料以 $\bar{x}\pm s$ 表示,组间比较采用t检验。偏态分布的计量资料以M(范围)表示,组间比较采用Mann-Whitney U检验。计数资料以绝对数表示,组间比较采用 χ^2 检验或Fisher确切概率法。等级资料组间比较采用Mann-Whitney U检验。 $P<0.05$ 为差异有统计学意义。

结 果

一、倾向评分匹配情况及匹配后两组病人一般资料比较

623例病人中,75例配对成功,其中ESD+TLDG组25例,TLDG组50例。倾向评分匹配后两组病人性别、年龄、BMI、肿瘤位置、肿瘤长径、临床分期、术前合并症一般资料比较,差异均无统计学意义($P>0.05$)。清除BMI、肿瘤长径、临床分期因素混杂偏倚,具有可比性。见表2。

二、TLDG术中和术后情况

倾向评分匹配后两组病人TLDG手术时间、术后引流管拔除时间比较,差异均有统计学意义($P<0.05$);TLDG术中出血量、淋巴结清扫数目、术后住院时间、围术期并发症比较,差异均无统计学意义

表2 ESD+TLDG组和TLDG组早期胃癌病人倾向评分匹配后一般资料比较

Table 2 Comparison of general data of early gastric cancer patients between totally laparoscopic distal gastrectomy after endoscopic submucosal dissection group and totally laparoscopic distal gastrectomy group

after propensity score matching

组别	例数	性别(例)		年龄 ($\bar{x}\pm s$,岁)	体质质量指数 ($\bar{x}\pm s$,kg/m ²)	肿瘤位置(例)		肿瘤长径(例)		
		男	女			胃中部	胃下部	≤20 mm	21~30 mm	>30 mm
ESD+TLDG组	25	17	8	59±11	22.3±3.6	9	16	16	6	3
TLDG组	50	30	20	62±11	23.6±2.9	24	26	29	12	9
统计值		$\chi^2=0.456$		$t=1.369$		$t=1.542$		$\chi^2=0.974$		$Z=-0.597$
P值		>0.05		>0.05		>0.05		>0.05		>0.05
组别		临床分期(例)			术前合并症(例)					
		I期	II期	III期	高血压病	冠心病	2型糖尿病	其他		
ESD+TLDG组	25	24	1	0	8	1	4	3		
TLDG组	50	48	2	0	19	3	9	2		
统计值		$Z=0.000$			$\chi^2=0.029$					
P值		>0.05			>0.05					

注:ESD+TLDG组早期胃癌病人行内镜黏膜下剥离术+全腹腔镜远端胃切除术,TLDG组早期胃癌病人行全腹腔镜远端胃切除术

表3 ESD+TLDG组和TLDG组早期胃癌病人倾向评分匹配后术中和术后情况比较

Table 3 Comparison of intraoperative and postoperative situations of early gastric cancer patients between totally laparoscopic distal gastrectomy after endoscopic submucosal dissection group and totally laparoscopic distal gastrectomy group after propensity score matchin

组别	例数	TLDG 手术时间 [M(范围), min]	术中出血量(例)			淋巴结清扫数目 [M(范围), 枚]	术后拔除引流管时间 [M(范围), d]
			<50 mL	50~100 mL	>100 mL		
ESD+TLDG 组	25	180(124~289)	7	9	9	34(16~58)	6(4~13)
TLDG 组	50	170(106~250)	18	26	6	39(22~68)	6(4~9)
统计值		Z=-2.396		Z=-1.703		Z=-1.958	Z=-3.039
P值		<0.05		>0.05		>0.05	<0.05

组别	例数	术后住院时间 [M(范围), d]	围术期并发症(例)			
			切口脂肪液化	术后胃瘫	吻合口出血	肺部感染
ESD+TLDG 组	25	8(6~31)	1	1	0	0
TLDG 组	50	8(6~29)	0	0	1	1
统计值		Z=-1.139			$\chi^2=0.033$	
P值		>0.05			>0.05	

注:ESD+TLDG 组早期胃癌病人行内镜黏膜下剥离术+全腹腔镜远端胃切除术,TLDG 组早期胃癌病人行全腹腔镜远端胃切除术;

TLDG 为全腹腔镜远端胃切除术

($P>0.05$)。见表3。发生吻合口出血病人经内镜下止血后缓解,其余并发症病人经保守治疗后均缓解。

三、ESD+TLDG 组病人分层分析

5例ESD后≤14 d行TLDG病人与20例ESD后>14 d行TLDG病人,TLDG手术时间,术中出血量(<50 mL、50~100 mL、>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为200 min(170~289 min),0、3、2例,36枚(9~57枚),7 d(5~9 d),8 d(7~9 d),1例和180 min(124~253 min),8、6、6例,34枚(8~78枚),6 d(4~13 d),8 d(6~31 d),1例,TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=-1.536$, -1.993 , -0.238 , -0.932 , -0.589 , $P>0.05$),围术期并发症比较,差异无统计学意义($P>0.05$)。

13例ESD后≤21 d行TLDG病人与12例ESD后>21 d行TLDG病人,TLDG手术时间,术中出血量(<50 mL、50~100 mL、>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为200 min(145~289 min),2、6、5例,34枚(8~57枚),6 d(4~11 d),8 d(6~11 d),1例和179 min(124~240 min),6、3、3例,34枚(16~78枚),6 d(5~13 d),8 d(6~31 d),1例;TLDG手术时间比较,差异有统计学意义($Z=-2.241$, $P<0.05$),TLDG术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=$

-1.471,-0.163,-0.084,-0.194, $P>0.05$),围术期并发症比较,差异无统计学意义($P>0.05$)。

15例ESD后<28 d行TLDG病人与10例ESD后>28 d行TLDG病人,TLDG手术时间,术中出血量(<50 mL、50~100 mL、>100 mL),淋巴结清扫数目,术后引流管拔除时间,术后住院时间,围术期并发症分别为190 min(145~289 min),2、7、6例,33枚(8~57枚),6 d(4~11 d),8 d(6~31 d),1例和179 min(124~240 min),6、2、2例,37枚(16~78枚),6 d(5~13 d),8 d(6~14 d),1例,TLDG手术时间、术中出血量、淋巴结清扫数目、术后引流管拔除时间、术后住院时间比较,差异均无统计学意义($Z=-1.619$, -2.000 , -0.667 , -0.370 , -0.057 , $P>0.05$),围术期并发症比较,差异无统计学意义($P>0.05$)。

讨 论

一、早期胃癌 ESD 非治愈性切除后治疗策略

近年来,随着诊断技术的不断进步,早期胃癌检出率不断提高^[10~11]。对于早期胃癌淋巴结转移风险低的病人,通常行ESD治疗。然而,有研究结果显示:6.6%~28.4%病人行ESD后,未能达到治愈性切除标准^[7,12~16]。对于这部分病人,目前主要采取再次行ESD或行外科手术治疗,其选择主要取决于2个方面:(1)残留肿瘤风险^[17]。(2)淋巴结转移可能^[18~19]。日本胃癌协会第5版《胃癌治疗指南》建

议:早期胃癌行 ESD 非治愈性切除后,淋巴结转移风险较高的病人应追加外科手术治疗^[2]。大多数临床研究证据也支持该决策^[20-26]。2014—2019 年,359 例病人因胃腺癌在南京医科大学第一附属医院消化内镜中心行 ESD 治疗,95 例经术后组织病理学检查证实为非治愈性 ESD,其中 47 例在我科追加行根治性手术,25 例手术方式为 TLDG,即本研究中 ESD+TLDG 组病人。

有研究结果显示:早期胃癌术前采用 CT 检查评估淋巴结转移的方法并不准确^[27-28]。日本早期胃癌治疗共识制定协会 2017 年提出:通过 eCura 评分预测早期胃癌淋巴结转移风险模型,根据肿瘤长径(>3 cm 计 1 分)、浸润深度(SM2 计 1 分)、淋巴管侵犯(阳性计 3 分)、脉管侵犯(阳性计 1 分)和垂直切缘(阳性计 1 分)5 个因素将早期胃癌淋巴结转移风险分为低(0~1 分)、中(2~4 分)、高(5~7 分)3 组,并建议中、高危组追加根治手术,这可以作为 ESD 术后追加根治性手术的指导方案^[29]。

另外,由于 ESD 术后产生的瘢痕范围大于病变范围,且 ESD 产生的溃疡在愈合期间切除部位组织收缩,所以在相同情况下,追加手术的切除范围通常要大于未行 ESD 病人的切除范围^[30-31]。Aoyama 等^[32]的单中心回顾性研究结果显示:ESD 对后续根治手术的切除方案会产生影响。但尚缺乏更高级别的临床研究进行验证。

二、早期胃癌 ESD 后行腹腔镜远端胃切除术疗效

Suzuki 等^[33]的研究结果显示:早期胃癌 ESD 后行腹腔镜辅助远端胃切除术病人,吻合口漏和胰瘘发生率均为 16%。本研究结果显示:ESD+TLDG 组和 TLDG 组病人 TLDG 手术时间、术后引流管拔除时间比较,差异均有统计学意义;而术中出血量、淋巴结清扫数目、术后住院时间、围术期并发症比较,差异均无统计学意义。笔者认为:早期胃癌行 ESD,会延长后续行 TLDG 的手术时间和术后引流管拔除时间,但不影响病人近期疗效。

三、早期胃癌 ESD 后行外科手术治疗时间间隔的选择

目前,早期胃癌 ESD 后追加行外科手术治疗的时间间隔尚无标准。本研究分层分析结果显示:ESD 后不同时间间隔行 TLDG 病人,仅 ESD 后≤21 d 和>21 d 行 TLDG 病人的 TLDG 手术时间比较,差异

有统计学意义。有研究结果显示:ESD 后 6~8 周,手术创面可愈合或形成瘢痕组织^[34-37]。本研究中,未纳入 TLDG 术中组织粘连情况。笔者认为:ESD 后,在较短时间内间隔内追加行外科手术,会受到因 ESD 引起组织损伤形成粘连,导致组织水肿和溃疡,以及活动性炎症的不利影响。这可能是 ESD 后≤21 d 和>21 d 行 TLDG 的病人,TLDG 手术时间差异有统计学意义的原因。有研究结果显示:抗溃疡治疗和根除幽门螺杆菌可促进 ESD 后,手术部位溃疡愈合^[38]。因此,笔者建议:ESD 后,可常规行抗溃疡和根除幽门螺杆菌治疗。

四、本研究局限性

本研究为单中心回顾性研究,样本量较小,时间跨度较长。此外,本研究仅纳入肿瘤位置为胃中、下部病人,未纳入全胃癌和近端胃癌病人,研究结果不全面,今后需开展多中心、大样本临床研究进一步验证。

综上,与直接行 TLDG 比较,早期胃癌行 ESD+TLDG 会延长 TLDG 手术时间和术后引流管拔除时间,但不影响近期疗效;早期胃癌 ESD 后≤21 d 行 TLDG 与>21 d 行 TLDG 手术时间比较,差异有统计学意义。

利益冲突 所有作者均声明不存在利益冲突

参 考 文 献

- [1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2018, 68(6):394-424. DOI:10.3322/caac.21492.
- [2] Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition)[J]. Gastric Cancer, 2021, 24(1):1-21. DOI:10.1007/s10120-020-01042-y.
- [3] Noh GY, Ku HR, Kim YJ, et al. Clinical outcomes of early gastric cancer with lymphovascular invasion or positive vertical resection margin after endoscopic submucosal dissection[J]. Surg Endosc, 2015, 29(9):2583-2589. DOI:10.1007/s00464-014-3973-0.
- [4] Oka S, Tanaka S, Kaneko I, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer[J]. Gastrointest Endosc, 2006, 64(6):877-883. DOI:10.1016/j.gie.2006.03.932.
- [5] Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) guideline[J]. Endoscopy, 2015, 47(9):829-854. DOI:10.1055/s-0034-1392882.
- [6] Kim HJ, Kim SG, Kim J, et al. Clinical outcomes of early gastric cancer with non-curative resection after patholo-

- gical evaluation based on the expanded criteria[J]. PLoS One, 2019, 14(10): e0224614. DOI: 10.1371/journal.pone.0224614.
- [7] Lee H, Lee HH, Song KY, et al. Negative impact of endoscopic submucosal dissection on short-term surgical outcomes of subsequent laparoscopic distal gastrectomy for gastric cancer[J]. Ann Surg Oncol, 2020, 27(1): 313-320. DOI:10.1245/s10434-019-07962-z.
- [8] Ebihara Y, Okushiba S, Kurashima Y, et al. Totally laparoscopic gastrectomy for gastric cancer after endoscopic submucosal dissection: a propensity score matching analysis[J]. Langenbecks Arch Surg, 2015, 400(8): 967-972. DOI:10.1007/s00423-015-1349-0.
- [9] Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience[J]. Ann Surg, 2009, 250(2): 187-196. DOI: 10.1097/SLA.0b013e3181b13ca2.
- [10] Sumiyama K. Erratum to: past and current trends in endoscopic diagnosis for early stage gastric cancer in Japan[J]. Gastric Cancer, 2017, 20(3): 562. DOI: 10.1007/s10120-017-0711-z.
- [11] Jung KW, Won YJ, Oh CM, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2014[J]. Cancer Res Treat, 2017, 49(2): 292-305. DOI: 10.4143/crt.2017.118.
- [12] Tanabe S, Hirabayashi S, Oda I, et al. Gastric cancer treated by endoscopic submucosal dissection or endoscopic mucosal resection in Japan from 2004 through 2006: JGCA nationwide registry conducted in 2013[J]. Gastric Cancer, 2017, 20(5): 834-842. DOI: 10.1007/s10120-017-0699-4.
- [13] Sunagawa H, Kinoshita T, Kaito A, et al. Additional surgery for non-curative resection after endoscopic submucosal dissection for gastric cancer: a retrospective analysis of 200 cases[J]. Surg Today, 2017, 47(2): 202-209. DOI: 10.1007/s00595-016-1353-1.
- [14] 李韶华, 谢华红, 玄立萍, 等. 内镜黏膜下剥离术治疗早期胃癌复发及影响因素分析[J]. 临床误诊误治, 2019, 32(9): 58-61. DOI:10.3969/j.issn.1002-3429.2019.09.015.
- [15] 金超琼, 应笑, 吕宾. 早期胃癌内镜下非治愈性切除患者淋巴结转移的危险因素[J]. 中华消化杂志, 2020, 40(3): 208-211. DOI:10.3760/cma.j.issn.0254-1432.2020.03.015.
- [16] 褚宇宁, 毛涛, 荆雪, 等. 未分化型早期胃癌内镜黏膜下剥离术扩大适应证的可行性探讨[J]. 中华消化杂志, 2020, 40(1): 30-35. DOI:10.3760/cma.j.issn.0254-1432.2020.01.006.
- [17] Tian YT, Ma FH, Wang GQ, et al. Additional laparoscopic gastrectomy after noncurative endoscopic submucosal dissection for early gastric cancer: a single-center experience[J]. World J Gastroenterol, 2019, 25(29): 3996-4006. DOI:10.3748/wjg.v25.i29.3996.
- [18] 周红, 郭春光, 陈应泰, 等. 早期胃癌非治愈性内镜黏膜下剥离术后的治疗策略研究[J]. 中华肿瘤杂志, 2019, 41(11): 865-869. DOI:10.3760/cma.j.issn.0253-3766.2019.11.012.
- [19] Akaike H, Kawaguchi Y, Shiraishi K, et al. Validity of additional surgical resection by comparing the operative risk with the stratified lymph node metastatic risk in patients with early gastric cancer after endoscopic submucosal dissection[J]. World J Surg Oncol, 2019, 17(1): 136. DOI:10.1186/s12957-019-1679-4.
- [20] Jeon MY, Park JC, Hahn KY, et al. Long-term outcomes after noncurative endoscopic resection of early gastric cancer: the optimal time for additional endoscopic treatment[J]. Gastrointest Endosc, 2018, 87(4): 1003-1013.e2. DOI:10.1016/j.gie.2017.10.004.
- [21] Suzuki S, Gotoda T, Hatta W, et al. Survival benefit of additional surgery after non-curative endoscopic submucosal dissection for early gastric cancer: a propensity score matching analysis[J]. Ann Surg Oncol, 2017, 24(11): 3353-3360. DOI:10.1245/s10434-017-6039-4.
- [22] Suzuki H, Oda I, Abe S, et al. Clinical outcomes of early gastric cancer patients after noncurative endoscopic submucosal dissection in a large consecutive patient series[J]. Gastric Cancer, 2017, 20(4): 679-689. DOI:10.1007/s10120-016-0651-z.
- [23] Kikuchi S, Kuroda S, Nishizaki M, et al. Management of early gastric cancer that meet the indication for radical lymph node dissection following endoscopic resection: a retrospective cohort analysis[J]. BMC Surg, 2017, 17(1): 72. DOI:10.1186/s12893-017-0268-0.
- [24] Kawata N, Kakushima N, Takizawa K, et al. Risk factors for lymph node metastasis and long-term outcomes of patients with early gastric cancer after non-curative endoscopic submucosal dissection[J]. Surg Endosc, 2017, 31(4): 1607-1616. DOI:10.1007/s00464-016-5148-7.
- [25] Hatta W, Gotoda T, Oyama T, et al. Is the eCura system useful for selecting patients who require radical surgery after noncurative endoscopic submucosal dissection for early gastric cancer? A comparative study[J]. Gastric Cancer, 2018, 21(3): 481-489. DOI:10.1007/s10120-017-0769-7.
- [26] Hatta W, Gotoda T, Oyama T, et al. Is radical surgery necessary in all patients who do not meet the curative criteria for endoscopic submucosal dissection in early gastric cancer? A multi-center retrospective study in Japan[J]. J Gastroenterol, 2017, 52(2): 175-184. DOI: 10.1007/s00535-016-1210-4.
- [27] Wada T, Yoshikawa T, Kamiya A, et al. A nodal diagnosis by computed tomography is unreliable for patients who need additional gastrectomy after endoscopic submucosal dissection[J]. Surg Today, 2020, 50(9): 1032-1038. DOI:10.1007/s00595-020-01985-w.
- [28] Ju MR, Karalis JD, Blackwell JM, et al. Inaccurate clinical stage is common for gastric adenocarcinoma and is associated with undertreatment and worse outcomes[J]. Ann Surg Oncol, 2021, 28(5): 2831-2843. DOI:10.1245/s10434-020-09403-8.
- [29] Hatta W, Gotoda T, Oyama T, et al. A scoring system to stratify curability after endoscopic submucosal dissection for early gastric cancer: "ecura system"[J]. Am J Gastroenterol, 2017, 112(6): 874-881. DOI:10.1038/ajg.2017.95.
- [30] Kawata N, Kakushima N, Tokunaga M, et al. Influence of endoscopic submucosal dissection on additional gastric resections[J]. Gastric Cancer, 2015, 18(2): 339-345. DOI:10.1007/s10120-014-0379-6.
- [31] Ishida R, Kanaji S, Maehara R, et al. Significance of additional gastrectomy including endoscopic submucosal dissection scar for gastric cancer[J]. Anticancer Res, 2018, 38(9): 5289-5294. DOI:10.21873/anticanres.12855.
- [32] Aoyama J, Sakuramoto S, Miyawaki Y, et al. Impact of endoscopic resection on the choice of surgical procedure in patients with additional laparoscopic gastrectomy[J].

- Gastric Cancer, 2020, 23(5):913-921. DOI:10.1007/s10120-020-01057-5
- [33] Suzuki T, Tanabe K, Vu DTA, et al. Safety and efficacy of laparoscopy-assisted gastrectomy after endoscopic submucosal dissection for early gastric cancer: a retrospective report[J]. J Cancer Therapy, 2013, 4(1):54-60. DOI:10.4236/jct.2013.41A008.
- [34] Tsuchiya I, Kato Y, Tanida E, et al. Effect of vonoprazan on the treatment of artificial gastric ulcers after endoscopic submucosal dissection: prospective randomized controlled trial[J]. Dig Endosc, 2017, 29(5):576-583. DOI:10.1111/den.12857.
- [35] Tomita T, Kim Y, Yamasaki T, et al. Prospective randomized controlled trial to compare the effects of omeprazole and famotidine in preventing delayed bleeding and promoting ulcer healing after endoscopic submucosal dissection[J]. J Gastroenterol Hepatol, 2012, 27(9):1441-1446. DOI:10.1111/j.1440-1746.2012.07144.x.
- [36] Higuchi K, Takeuchi T, Uedo N, et al. Efficacy and safety of 1-week helicobacter pylori eradication therapy and 7-week rebamipide treatment after endoscopic submucosal dissection of early gastric cancer in comparison with 8-week PPI standard treatment: a randomized, controlled, prospective, multicenter study[J]. Gastric Cancer, 2015, 18(3): 612-617. DOI: 10.1007/s10120-014-0404-9.
- [37] Akagi T, Shiraishi N, Hiroishi K, et al. Case series of intra-abdominal adhesions induced by artificial ulceration after endoscopic submucosal dissection before additional laparoscopic gastrectomy[J]. Gastrointest Endosc, 2010, 72(2):438-443. DOI:10.1016/j.gie.2010.03.1066
- [38] Shimozato A, Sasaki M, Ogasawara N, et al. Risk factors for delayed ulcer healing after endoscopic submucosal dissection of gastric neoplasms[J]. J Gastrointest Liver Dis, 2017, 26(4):363-368. DOI: 10.15403/jgld.2014.1121.264.

消化外科云学院——菁英在线会议通知

尊敬的各位同道：

大家好！

由《中华消化外科杂志》编辑委员会主办，辉瑞投资有限公司承办的“消化外科云学院——菁英在线”项目已于2020年8月隆重举行。

该项目汇聚《中华消化外科杂志》菁英荟青年专家力量，发挥《中华消化外科杂志》编辑委员会引领作用，推动我国消化外科手术操作规范化和标准化，提高临床中青年医师围术期管理质量，全面深入贯彻加速康复外科理念。该项目通过线上网络直播覆盖、精彩病例视频展示、知名专家互动探讨等形式，旨在为全国消化外科同道搭建一个良好的学术交流互动平台。

该项目以“知行合一，融汇创新”为主题，将围绕肝、胆、胰、胃、肠、移植外科

前沿技术发展、理念创新、外科医师培训、多学科团队协作等领域，融合全媒体，

开启互联网+医疗学术风暴，助推我国消化外科事业的可持续发展，普惠全国消化外科同道。

诚挚邀请您参与“消化外科云学院——菁英在线”，我们携手共促远程医学，
共享优质资源，共建健康中国。



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