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分析胃肠 ESD 治疗早期胃癌疗效、随访情况及血清胃蛋白酶原、癌胚抗原表达水平 *

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摘要 目的:分析予以早期胃癌患者胃肠内镜下黏膜剥离术(ESD)治疗的效果,为此类患者治疗提供参考。**方法:**于我院诊治的早期胃癌患者中筛选 60 例为主体,以电脑随机法将患者分成常规组(30 例)、实验组(30 例)。予以常规组外科切除术治疗,予以实验组胃肠 ESD 治疗,完成治疗后对比各组临床疗效、手术指标、血清肿瘤标志物、PG 水平(PG I、PG II)、随访情况,病例选取时间为 2019 年 11 月-2021 年 11 月。**结果:**实验组患者治疗总有效率与常规组对比无差异($P>0.05$);治疗前两组患者的 CEA、CA199、CA125 水平无差异($P>0.05$),治疗后两组患者的 CEA、CA199、CA125 水平均降低,并且实验组患者降低幅度大于常规组($P<0.05$);实验组患者的手术时间、出血量、住院时间、输血率少于或小于常规组患者相应指标($P<0.05$);治疗前两组患者的 PG I、PG II、PG I/PG II 水平无差异($P>0.05$),治疗后两组患者的 PG I、PG I/PG II 水平均升高,PG II 水平降低,实验组患者变化幅度大于常规组($P<0.05$);实验组复发率与常规组比较无差异($P<0.05$)。**结论:**胃肠 ESD 治疗早期胃癌患者的效果较为理想,可有效改善血清蛋白酶原及肿瘤标志物水平,具有出血量少、手术时间短等优势,同时还可降低并发症风险,可在此类疾病治疗中应用并推广。

关键词:胃肠 ESD;早期胃癌;疗效;随访情况;血清胃蛋白酶原;癌胚抗原

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Analysis of the Curative Effect, Follow-up and Serum Pepsinogen and Carcinoembryonic Antigen Expression Levels of Gastrointestinal ESD in The Treatment of Early Gastric Cancer*

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ABSTRACT Objective: To analyze the efficacy of endoscopic submucosal dissection (ESD) in the treatment of early gastric cancer, and to provide reference for the treatment of such patients. **Methods:** 60 patients with early gastric cancer were selected as the main body. The patients were randomly divided into routine group (30 cases) and experimental group (30 cases). The patients were treated with surgical resection in the routine group and gastrointestinal ESD in the experimental group. After treatment, the clinical efficacy, surgical indicators, serum tumor markers, PG levels (PG I, PG II) and follow-up were compared in each group. The case selection time was from November 2019 to November 2021. **Results:** There was no difference between the total effective rate of patients in the experimental group and the routine group ($P>0.05$); There was no difference in the levels of CEA, CA199 and CA125 between the two groups before treatment ($P>0.05$). After treatment, the levels of CEA, CA199 and CA125 in the two groups decreased, and the decrease in the experimental group was greater than that in the conventional group ($P<0.05$); The operation time, blood loss, hospitalization time and blood transfusion rate of the experimental group were less than or less than those of the conventional group ($P<0.05$); Before treatment, there was no difference in the levels of PG I, PG II and PG I /pg II between the two groups ($P>0.05$). After treatment, the levels of PG I, PG I /pg II in the two groups increased, and the level of PG II decreased. The range of change in the experimental group was greater than that in the conventional group($P<0.05$); The recurrence rate of the experimental group was similar with the conventional group ($P>0.05$). **Conclusion:** the effect of gastrointestinal ESD in the treatment of patients with early gastric cancer is ideal, which can effectively improve the level of serum proteasome and tumor markers. It has the advantages of less bleeding and short operation time. At the same time, it can also reduce the risk of complications, which can be applied and promoted in the treatment of such diseases.

Key words: Gastrointestinal ESD; Early gastric cancer; Curative effect; Follow up; Serum pepsinogen; Carcinoembryonic antigen

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前言

胃癌属于临床较为常见的肿瘤疾病,可发生于胃的任何部位,其中 50% 的胃癌会发生在胃窦部、胃大弯、胃小弯、胃前壁、胃后壁,疾病预后和胃癌分期、发生部位、治疗措施、组织类型存在较大关系^[1,2]。早期胃癌(Early gastric cancer, EGC)多存在于黏膜下层、黏膜层的,大部分患者无淋巴结转移情况,由于临床症状轻微或无症状,极易错失最佳治疗时机^[3,4]。随着医疗技术的快速进展,早期胃癌检出率明显提升,越来越多的患者可在早期得到有效治疗^[4]。对于早期胃癌的治疗,临床多采取根治性手术切除治疗,虽可切除病变,提高机体生存率,但此种治疗方案存在创伤性大、术后并发症多、胃部解剖结构破坏等缺点^[5,6]。随着医疗技术的进步,胃肠内镜下黏膜剥离术(Endoscopic submucosal dissection, ESD)被应用于早期胃癌的治疗中,明显减少了手术创伤,且对胃部解剖结构的影响较小,术后并发症较少,应用优势较为显著^[7,8]。本文筛选我院 2019 年 11 月 -2021 年 11 月诊疗的 60 例早期胃癌患者为对象实施对照分析,旨在评价胃肠 ESD 治疗对于患者临床疗效、手术指标、血清肿瘤标志物、PG 水平等指标的影响,内容如下。

1 资料与方法

1.1 一般资料

研究日期是 2019 年 11 月 -2021 年 11 月,以本院诊疗的 60 例早期胃癌患者为主体,应用电脑随机法分组,其中 30 例纳入常规组,剩余 30 例纳入实验组。常规组年龄是 24~79 岁,均值(51.52 ± 4.75)岁;男女比例为 17/13;病程是 2~5 个月,平均(3.58 ± 0.75)个月。实验组年龄是 25~78 岁,均值(51.58 ± 4.74)岁;男女比例为 18/12;病程是 3~4 个月,平均(3.54 ± 0.79)个月。应用 SPSS24.0 软件分析资料,确定差异无意义, ($P > 0.05$)。

1.2 研究标准

纳入标准:患者诊疗资料完整,可保证研究顺利实施;签署知情同意书,满足伦理道德要求,符合《世界医学会赫尔辛基宣言》原则^[9];病理活检确诊,均无淋巴结转移来满足 ESD 适应证。

排除标准:血液系统及传染性疾病;严重肝肾功能疾病;自身代谢性疾病;免疫系统疾病;精神类疾病或者认知功能异常;难以耐受麻醉、手术;其他肿瘤疾病。

1.3 研究方法

予以常规组外科切除术治疗,由一名医生外科医生实施操作,严格遵循肿瘤根治原则,依据患者肿瘤部位选择适宜切除方法,如胃大部近端根治性切除术、全胃切除术、胃大远端根治

性切除术,将标本送至病理科实施组织学检查。

实验组采取胃肠 ESD 治疗,具体为:通过胃镜确定病变部位,以其他内镜技术确定病变范围,确认无误后通过电凝对于距离病变 5 mm 的部位实施顺时针、逆时针标记,以环形点状标记,标记点间隔距离一般为 2 mm 左右。在病灶边缘标记点位置外侧黏膜下注射适量的含肾上腺素,多处注射以抬举病变。环形切开病变周围黏膜组织,沿标记点外缘切开胃黏膜,切至胃黏膜下层,首先切开病变肛侧黏膜、病变口侧,切开过程中需要避免累及病变组织。将透明帽安装在内镜镜头上,根据患者实际情况选择 Dual 刀、IT 刀,对于黏膜实施剥离,完整、大块切除病灶。剥离黏膜时需要根据实际情况多次补充黏膜下注射液,若剥离血管较为丰富的黏膜肌层,可增加出血风险,故需要注意及时采取金属夹、电凝止血。完整切除病变后,应用电凝、金属夹对创面实施止血处理,将标本送至病理科实施组织学检查。

1.4 观察指标

(1)临床疗效。以实体瘤疗效评价标准评价临床疗效^[10,11],标准为完全缓解(Complete remission, CR)、部分缓解(Partial remission, PR)、疾病进展(Progressive disease, PD)、疾病稳定(Stable disease, SD)。总有效率=(CR+PR)总数/100%。

(2)血清肿瘤标志物^[12,13]。测定各组患者治疗前后的血清癌胚抗原(Carcinoembryonic antigen, CEA)、糖类抗原 125(Carbohydrate antigen 125, CA125)、糖类抗原 199(Carbohydrate antigen 199, CA199)水平,通过全自动化学发光免疫分析仪检测。

(3)手术指标。对比各组手术时间、出血量、住院时间、输血率。

(4)胃蛋白酶原(Pepsinogen, PG)水平^[14,15]。抽取患者术前、术后 7 d 的静脉血,离心处理后采取酶联免疫吸附法测定 PG I、PG II、PG I/PG II 水平。

(5)随访情况。全部患者均进行跟踪随访,随访率为 100%,随访时间为术后 6 个月,了解患者复发情况。

1.5 统计学方法

采用 SPSS23.0 分析,运用[n/(%)]表示计数资料,采用(χ^2)或 Fisher 检验,计量资料采用($\bar{x} \pm s$)表示,采用 t 检验,取 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗总有效率比较

实验组患者治疗总有效率达 90.00%,常规组患者治疗总有效率达 93.34%,实验组患者治疗总有效率与常规组对比无差异($P > 0.05$),见表 1。

表 1 两组患者治疗总有效率比较[n/(%)]

Table 1 Comparison of total effective rate between the two groups [n/(%)]

Groups	CR	PR	SD	PD	Total effective rate
Experimental group (n=30)	15 (50.00)	12 (40.00)	2 (6.67)	1 (3.33)	27 (90.00)
Regular group (n=30)	17 (56.67)	11 (36.67)	1 (3.33)	1 (3.33)	28 (93.34)
χ^2	--	--	--	--	--
P	--	--	--	--	--

- 2.2 两组患者治疗前后血清肿瘤标志物水平比较 0.05), 治疗后两组水平均降低, 并且实验组患者降低幅度大于治疗前两组患者的 CEA、CA199、CA125 水平无差异($P>$ 常规组($P<0.05$), 见表 2。

表 2 两组患者治疗前后血清肿瘤标志物水平比较($\bar{x} \pm s$)Table 2 Comparison of serum tumor markers between the two groups before and after treatment($\bar{x} \pm s$)

Groups	Time	Experimental group(n=30)	Regular group(n=30)	t	P
CEA(ng/mL)	Before treatment	13.28± 3.38	13.36± 3.49	0.090	0.928
	After treatment	5.05± 0.62	5.45± 0.56	2.622	0.011
CA199(KU/L)	Before treatment	102.38± 12.35	102.72± 12.53	0.105	0.916
	After treatment	65.48± 9.19	70.28± 8.68	2.079	0.042
CA125(KU/L)	Before treatment	72.62± 7.21	72.42± 7.45	0.105	0.916
	After treatment	43.74± 5.46	46.94± 5.68	2.224	0.030

- 2.3 两组患者手术指标比较 者相应指标($P<0.05$), 见表 3。
实验组患者的手术时间等手术指标少于或小于常规组患

表 3 两组患者手术指标比较($\bar{x} \pm s$)Table 3 Comparison of surgical indicators between the two groups($\bar{x} \pm s$)

Groups	Operation time(min)	Bleeding volume(mL)	Length of stay(d)	Transfusion rate(%)
Experimental group(n=30)	46.58± 11.39	52.39± 9.75	8.03± 1.02	0(0.00)
Regular group(n=30)	175.93± 33.02	102.36± 15.48	13.79± 1.56	4(13.33)
t	28.294	16.351	9.117	4.285
P	<0.001	<0.001	<0.001	0.038

- 2.4 两组患者治疗前后 PG 水平比较 均升高, PG II 水平降低, 实验组患者变化幅度大于常规组($P<$
治疗前两组患者的 PG I、PG II、PG I/PG II 水平差异无统 0.05), 见表 4。
计学意义($P>0.05$), 治疗后两组患者的 PG I、PG I/PG II 水平

表 4 两组患者治疗前后 PG 水平比较($\bar{x} \pm s$)Table 4 Comparison of PG levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	PG I (ug/L)		PG II (ug/L)		PG I /PG II	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group(n=30)	65.93± 6.58	93.26± 9.61	24.38± 2.97	15.49± 2.01	2.67± 0.35	5.98± 0.67
Regular group(n=30)	65.49± 6.29	87.34± 9.52	24.73± 2.85	17.36± 2.16	2.71± 0.32	4.17± 0.74
t	0.264	2.397	0.465	3.471	0.461	9.931
P	0.792	0.019	0.643	0.001	0.645	0.000

2.5 两组患者随访情况比较

术后随访结果显示, 实验组发生 1 例复发, 复发率是 3.33%, 常规组发生 3 例复发, 复发率是 10.00%, 实验组复发率与常规组比较无差异($\chi^2=0.268, P=0.605$)。

3 讨论

胃癌的死亡率、恶性程度均极高, 是临床发生率较高的一种消化系统肿瘤, 相关报道显示, 胃癌发病率位居全球第五, 死亡率位居第三^[16,17]。近年来, 受饮食习惯、生活方式等因素改变影响, 我国胃癌的发生率不断升高, 严重影响居民身心健康、生

活质量。早期胃癌并不会会有特异性症状, 该疾病的常规检查手段是电子胃镜, 但因民众体检意识较差, 导致很多胃癌在临床诊断时被发现已处于进展期胃癌, 错过了疾病的最佳治疗时机。报道显示: 使用手术、放化疗等手段治疗进展期胃癌, 其 5 年生存率不到 50%, 甚至更少, 但是早期胃癌经规范治疗后, 5 年生存率高达 90%以上^[18-20]。基于此, 可知对于早期胃癌, 早发现、早诊断、早治疗是提高其患者存活率的主要手段, 既往主要采取外科手术进行治疗, 虽具有较高的治疗有效率, 但将会对患者造成较大创伤, 且手术时间较长, 较高的经济费用给家庭带来负担。随着科技的不断发展, 医疗技术也随之更新换代, 内

镜下切除已逐渐成为治疗早期胃癌的重要方式,且临床显示疗效较外科手术优^[21-23]。

本次研究中,实验组患者治疗总有效率高达 90.00 %,复发率为 3.33 %,常规组患者治疗总有效率高达 93.34 %,复发率为 10.00 %,实验组患者治疗总有效率及复发率与常规组对比无差异,且研究组治疗后的 CEA、CA199、CA125 水平低于常规组,手术时间与住院时间短于常规组,输血率低于常规组,出血量少于常规组,PG I、PG I/PG II 水平高于常规组,PG II 低于常规组,充分证实了胃肠 ESD 治疗早期胃癌的效果,可明显改善机体血清肿瘤标志物与蛋白酶原水平,明显减少手术创伤,应用价值更为显著。该结果与张庆瑞等人^[24]的报道具有一致性。分析可知:CEA 可与细胞质中进行合成,经由细胞膜至细胞外,进一步到周围体液中,恶性肿瘤患者的血清 CEA 水平往往高于健康者。CA199 作为 1 种极为常见的糖蛋白类肿瘤标志物,存在于胎儿肠、胃以及胰腺的上皮,但在健康成人的胰腺和胃中的表达水平极低,而在消化道恶性肿瘤患者中血清 CA199 水平会显著升高,在临床上主要用于鉴别诊断胃癌、胰腺癌以及结肠癌患者。CA125 在子宫内膜癌、胃癌等多种恶性肿瘤患者中具有较高的血清表达水平^[25]。PGI 主要由胃底腺的主细胞和颈黏液细胞分泌;除胃底腺以外,胃窦幽门腺和十二指肠 Brunner 腺也参与了 PG II 的合成。胃体黏膜萎缩时,往往引起 PGI 水平下降,而 PG II 水平则保持不变甚至升高,导致 PGR 相应降低,因此血清 PG 水平可以用于胃黏膜萎缩的诊断^[26]。在早期胃癌治疗中,胃肠 ESD 在治愈性切除率,术后复发、提供完整及准确病理等方面具有更为理想的效果^[27]。相较于外科切除手术治疗,胃肠 ESD 明显减少了创伤面积,缩短了住院时间,同时还可保留脏器结构完整性,降低术后复发、并发症风险^[28]。胃肠 ESD 为目前国内公认的降低淋巴结转移风险的治疗方案,已经逐渐成为取代外科切除手术的标准治疗方案,可切除局部病变黏膜,控制病变转移与发展,还可获得较好的组织病理,可明确病变范围与性质^[29]。胃肠 ESD 是建立在 EMR 基础上的新型内镜技术,通过 IT 刀、Dual 刀等工具完整切除病灶,能够一次性地剥离病变黏膜,基本无残留病灶情况,可明显降低术后复发风险,对减轻疾病损害,改善预后具有重要作用^[30]。

综上所述,采取胃肠 ESD 治疗早期胃癌患者的效果较为理想,可有效改善血清蛋白酶原及肿瘤标志物水平,具有出血量少、手术时间短等优势,同时还可降低并发症风险,可在此类疾病治疗中应用并推广。

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