JBUON 2019; 24(3): 1087-1091
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

Therapeutic effects of endoscopic mucosal resection on the recovery and prognosis of early gastric cancer

Tengfei Li, Pengfei Liu, Bin Xiang

Department of Gastroenterology, The Affiliated Jiangyin Hospital of Southeast University Medical School, Jiangyin, China.

Summary

Purpose: *To study the clinical effect of endoscopic mucosal resection (EMR) in the treatment of early gastric cancer (EGC), and to evaluate the recovery and prognosis, so as to provide references for clinical selection of treatment methods.*

Methods: *120 patients with EGC were selected and randomly divided into the EMR group and the radical surgery group. Before surgery and 3 days after surgery, the levels of traumatic response-related indexes in serum [adrenocorticotropic hormone (ACTH), cortisol (Cor), gastrin (GAS) and motilin (MTL)] were assessed. Before surgery, 3 months and 1 year after surgery, the expression levels of tumor markers [carcinoembryonic antigen (CEA), carbohydrate antigen 19.9 (CA19.9), CA125 and CA724] were assessed. Before surgery and 3 days and 3 months after surgery, the immune function indexes [cluster of differentiation (CD)25$^+$, CD28$^+$ and inducible costimulator (ICOS)] were measured. Moreover, the clinical effect of surgery and the incidence rate of complications were compared between the two groups, and patients were followed up for at least 2 years to evaluate their prognosis.*

Results: *The clinical cure rate of tumor resection was comparable in both groups, and the incidence rate of complications in the EMR group was significantly lower than that in the radical surgery group ($p<0.05$). The levels of tumor markers were significantly increased compared with those before surgery in both groups ($p<0.05$), but without significant differences between the two groups. Three days after surgery in the radical surgery group, ACTH and Cor were increased, while GAS and MTL were decreased, and the levels of immune indexes declined ($p<0.05$). In the EMR group, the above indexes had no significant differences compared with those before surgery. Three days after surgery, the survival and recurrence rate in the EMR group and the radical surgery group were 95.0% vs. 98.3% and 5.0% vs. 3.3%, respectively ($p>0.05$).*

Conclusions: *The treatment of EGC with EMR has comparable clinical effect and prognosis to the traditional radical surgery, which causes less damage to the body and gastrointestinal function and less inhibition on the immune function, so it is worthy of clinical application.*

Key words: *endoscopic mucosal resection, early gastric cancer, prognosis, radical surgery*

Introduction

The early gastric cancer (EGC) lesions are confined to the mucous layer or submucous layer, and it is of great importance to improve the clinical diagnosis rate of EGC. In the past, the preferred therapeutic method was radical surgery immediately once the disease was diagnosed, and the 5-year survival rate was up to 95%, but problems such as more postoperative complications and high hospitalization costs made this option problematic [1-3].

With the increasing maturity of endoscopic diagnosis and treatment techniques, the postoperative survival rate and quality of life of patients have been significantly improved via the complete lesion resection using endoscopic mucosal resection (EMR) [4,5].

In 1984 [6], EMR was applied by some researchers for the first time in the clearance of local lesions of EGC, and the resected tissues were

Corresponding author: Bin Xiang, BM. Department of Gastroenterology, The Affiliated Jiangyin Hospital of Southeast University Medical School, No.163, Shoushan Rd, Jiangyin, Jiangsu 214400, China.
Tel: +86013961618595, Email: xiangbin7317@163.com
Received: 22/10/2018; Accepted: 18/11/2018

pathologically examined to determine the depth of lesion infiltration, since which EMR, with the constant advance in endoscopic equipment and the increasing improvement of operation techniques, has developed from a method for EGC diagnosis to an important treatment means for gastric cancer lesions that have a low risk of lymph node metastasis and can be completely resected [7].

In this study, the clinical effects of EMR and radical resection in the treatment of EGC were studied, and the recovery and prognosis were evaluated, so as to provide references for clinical selection of treatment methods.

Methods

Participants included in the study

A total of 120 patients from our hospital with EGC were selected as the study cohort. They were diagnosed via gastroscopy and biopsy, while those complicated with organ dysfunction, tumors in other sites or mental disorders were excluded. Patients enrolled were randomly divided into the EMR group and the radical surgery group. The general data, such as gender and age, were comparable between the two groups. Patients signed informed consent before study entry. This study was approved by the ethics committee of The Affiliated Jiangyin Hospital of Southeast University Medical School.

Research methods

After the preoperative preparation was made, vital signs were monitored during surgery. In the EMR group, the EMR was performed using the Olympus GIF-H260 electronic gastroscope. Patients took local anesthetics, like lidocaine, before treatment, and pigment staining and narrow band imaging examination were performed when the gastroscope entered the lesion to determine the lesion site and cancer extent. The injection needle was inserted through the endoscopic biopsy channel, and the needle tip was pierced into the base of polyp for multipoint submucosal injection 2-3 mm away from the outer edge of the lesion. About 2-10 mL adrenaline with normal saline (1:10000) were injected each time to protrude the entire lesion (positive lifting sign), and the protrusion lesions were held using the electronic snare, followed by complete resection of lesions. The resected tissues were sent for pathological examination. In the radical surgery group, traditional proximal total gastrectomy was performed, and anti-inflammatory, hemostatic and other symptomatic support were given postoperatively.

Detection indexes

Before surgery and 3 days after surgery, the levels of serum adrenocorticotropic hormone (ACTH), cortisol (Cor) and gastrointestinal hormones, including gastrin (GAS) and motilin (MTL), were detected using the Multiscan FC full-automatic microplate reader (Thermo Fisher Scientific, Waltham, MA, USA). Before surgery, 3 months and 1 year after surgery, the levels of serum tumor markers [carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), CA125 and CA724] were detected via electrochemiluminescence. Before surgery, 3 days and 3 months after surgery, the serum immune function indexes [cluster of differentiation (CD)25^+, $CD28^+$ and inducible costimulator (ICOS)] were measured using the Partec CyFlow Cube flow cytometer (Partec, Nürnberg, Germany). During follow-up, gastroscopy was performed regularly, and the postoperative recurrence was monitored to evaluate the prognosis.

Statistics

SPSS 20.0 software (IBM, Armonk, NY, USA) was used for data analysis. T-test was used for the intergroup analysis of quantitative data, and chi-square test was adopted for the analysis of percentage data. $P<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of clinical data between the two groups

There were no significant differences in clinical data such as age, gender, pathologic type, depth of infiltration and diameter of lesion between the two groups, which were comparable (Table 1).

Content of serum tumor markers in both groups

The expressions of CEA, CA19.9, CA125 and CA724 were comparable before surgery in the radical surgery group and the EMR group. With

Table 1. Comparisons of clinical data between the two groups (n=60)

Group	*Gender*		*Age (years) mean±SD*	*Grade of differentiation*			*Depth of infiltration*		*Lesion diameter (cm) mean±SD*
	Male	*Female*		*Undifferentiated, n*	*Moderate, n*	*High, n*	*Intramucosal carcinoma, n*	*Submucosal carcinoma, n*	
EMR group	33	27	52.6±4.9	28	22	10	45	15	1.4±0.3
Radical surgery group	29	31	53.3±5.7	30	23	7	47	13	1.6±0.4

the passing of time, the levels of tumor markers increased significantly in both the EMR and the radical surgery group at 3 months and 1 year after surgery compared with those before surgery (p<0.05) (Table 2).

Comparisons of traumatic response-related indexes between the two groups

Before surgery and 3 days after surgery in the radical surgery group, the mean levels of ACTH and Cor were 14.3±1.9 *vs.* 445.2±6.2 pmol/L (p<0.0001) and 12.5±1.7 *vs.* 40.1±6.1 nmol/L, respectively (p<0.0001). After surgery, the levels of ACTH and Cor were higher than those before surgery, while the levels of GAS and MTL were lower than those before surgery. In the EMR group, these indexes had no significant differences after surgery compared with those before surgery, and the content of ACTH and Cor was significantly lower than that in the radical surgery group, while that of GAS and MTL was higher than that in the radical surgery group (p<0.05) (Table 3).

Table 2. Comparison of the mean content of serum tumor markers between the two groups (n=60)

Detection index	*EMR group*			*Radical surgery group*		
	Before surgery	*3 months after surgery*	*1 year after surgery*	*Before surgery*	*3 months after surgery*	*1 year after surgery*
CEA (μg/L)	31.2±5.5	6.9±0.8*	3.7±0.6*	36.9±6.2	7.9±0.8*	4.5±0.6*
CA199 (U/mL)	49.9±6.8	12.5±1.7*	6.3±0.9*	56.1±7.7	13.3±2.5*	7.2±0.9*
CA125 (U/mL)	82.2±9.5	25.5±5.3*	18.3±3.2*	91.1±10.8	24.6±4.8*	19.1±3.6*
CA724 (U/mL)	50.3±7.5	9.3±2.1*	5.5±0.9*	53.3±8.8	11.1±2.8*	5.3±0.8*

*p<0.05 *vs.* before surgery in the same group

Table 3. Comparisons of traumatic response-related indexes between the two groups (n=60)

Group	*Before surgery*				*3 days after surgery*			
	ACTH (pmol/L)	*Cor (nmol/L)*	*GAS (pg/mL)*	*MTL (pg/mL)*	*ACTH (pmol/L)*	*Cor (nmol/L)*	*GAS (pg/mL)*	*MTL (pg/mL)*
EMR group	15.2±2.1	11.8±2.2	85.3±18.6	275.8±56.3	20.6±2.6#	15.5±2.8#	110.3±20.4#	328.6±44.6#
Radical surgery group	14.3±1.9	12.5±1.7	90.1±22.8	280.5±50.8	445.2±6.2*	40.1±6.1*	76.6±10.3*	180.3±47.5*

*p<0.05 *vs.* before surgery in the same group, #p<0.05 *vs.* radical surgery group

Table 4. Comparisons of immune function indexes (mean) between the two groups (n=60)

Detection index	*EMR group*			*Radical surgery group*		
	Before surgery	*3 months after surgery*	*1 year after surgery*	*Before surgery*	*3 months after surgery*	*1 year after surgery*
$CD25^+$	6.78±1.01	7.12±1.23#	10.78±1.83*	6.58±0.82	4.88±0.84*	9.26±1.77*
$CD28^+$	37.55±5.25	39.17±6.12#	50.01±6.08*	39.23±6.66	31.16±5.03*	48.85±7.23*
ICOS	1.65±0.24	1.75±0.27#	2.49±0.55*	1.61±0.22	1.15±0.09*	2.68±0.44*

*p<0.05 *vs.* before surgery in the same group, #p<0.05 *vs.* radical surgery group

Table 5. Comparison of general surgical data between the two groups (n=60)

Group	*Time of operation (min)*	*Hospitalization duration (days)*	*Total resection rate (%)*	*Curative resection rate (%)*	*Incidence rate of complications (%)*
EMR group	123.1±28.4*	5.9±2.8*	95.0	85.0	8.3
Radical surgery group	106.2±29.6*	8.8±3.1*	100.0	91.6	25.0*

*p<0.05 *vs.* radical surgery group

Immune function indexes in both groups

Detection results of serum immune function indexes revealed that before surgery and 3 days after surgery in the radical surgery group, the mean levels of $CD25^+$, $CD28^+$ and ICOS were 6.58±0.82 *vs.* 4.88±0.84 (p<0.0001), 39.23±6.66 *vs.* 31.16±5.03 (p<0.0329) and 1.61±0.22 *vs.* 1.15±0.09 (p<0.0001), respectively. The levels of these indexes after surgery were lower than those before surgery in the radical surgery group, while there were no significant changes in the EMR group. With the passing of time, the levels of immune function indexes were significantly increased in both the EMR and radical surgery group at 3 months after surgery, compared with those before surgery (p<0.05) (Table 4).

Comparisons of surgery and complications between the two groups

The operation time in the EMR group was significantly increased compared with that in the radical surgery group, and the clinical cure rate of tumor resection was comparable in both groups, but the incidence rate of complications in the EMR group was lower (p<0.05), indicating that EMR can alleviate the stress response status, reduce the gastrointestinal injury caused by surgical trauma and benefit the body's functional recovery (Table 5).

Comparisons of survival and recurrence rate between the two groups

The survival rate and recurrence rate in the EMR and the radical surgery group were 95.0% *vs.* 98.3% and 5.0% *vs.* 3.3%, respectively, showing no statistically significant differences between the two groups (p>0.05).

Discussion

Some normal cells can turn cancerous under the action of a variety of internal and external stimuli, and the clinical detection of serum tumor markers can be used in the auxiliary diagnosis, evaluation of therapeutic effect and judgement of prognosis. CEA, CA19.9, CA125 and CA724 are well-recognized tumor markers for EGC [8]. In this study, the detection results of serum tumor markers revealed that the expressions of CEA, CA19.9, CA125 and CA724 were comparable before surgery in the radical surgery and the EMR group. With the passing of time, the levels of tumor markers were significantly increased in both the EMR and radical surgery group at 3 months and 1 year after surgery compared with those before surgery (p<0.05), showing no significant differences between the two groups, indicating that both the radical surgery and the EMR group can effectively eliminate the lesion and inhibit the development of tumor.

ACTH and Cor are endocrine hormones released by the adrenal cortex under stress states such as surgical trauma and their levels directly reflect the degree of trauma [9]. Under normal conditions, the gastrointestinal motility is regulated by GAS secreted by G cells in the gastric antrum and MTL secreted by Mo cells in the small intestine. Both gastrointestinal hormones obviously decline in the case of gastrointestinal mucosal ischemia and hypoxia caused by surgical trauma [10,11].

An obvious advantage of endoscopic resection is the reduction of surgical trauma-induced stress response [12]. In this experiment, it was found that before surgery and at 3 days after surgery in the radical surgery group, the mean levels of ACTH and Cor were 14.3±1.9 *vs.* 445.2±6.2 pmol/L (p<0.0001) and 12.5±1.7 *vs.* 40.1±6.1 nmol/L (p<0.0001), respectively. After surgery, the levels of ACTH and Cor were higher than those before surgery, while the levels of GAS and MTL were lower than those before surgery. In the EMR group, these indexes had no significant differences after surgery compared with those before surgery, and the content of ACTH and Cor was significantly lower than that in the radical surgery group, while that of GAS and MTL was higher than that in the radical surgery group (p<0.05). Moreover, the comparison of clinical data between the two groups showed that the operation time in the EMR group was significantly increased compared with that in the radical surgery group, and the clinical cure rate of tumor resection was comparable in both groups, but the incidence rate of complications in the EMR group was significantly lower (p<0.05), suggesting that EMR can alleviate the stress response status, reduce the gastrointestinal injury caused by surgical trauma and benefit the body's functional recovery.

The severe inhibition of normal immune function is one of the negative important mechanisms of gastric cancer, which is manifested as significantly decreased expressions of immune molecules, such as CD25, CD28 and ICOS. The radical resection of tumor tissues can improve the immune function, but the laparotomy can lead to postoperative immune dysfunction [13,14]. As a minimally-invasive surgery, EMR can reduce the impact on immune function. In this study, the results of serum immune function indexes revealed that before surgery and 3 days after surgery in the radical surgery group, the mean levels of $CD25^+$, $CD28^+$ and ICOS were 6.58±0.82 *vs.* 4.88±0.84, 39.23±6.66 *vs.* 31.16±5.03 and 1.61±0.22 *vs.* 1.15±0.09, respectively. The levels of these indexes after surgery were lower than those before surgery in the radical surgery group,

while there were no significant changes in the EMR group. With the passing of time, the levels of immune function indexes were significantly increased in both groups at 3 months after surgery compared with those before surgery ($p<0.05$), displaying no significant differences between the two groups and indicating that EMR has little effect on the short-term immune function of patients after surgery compared with radical surgery. Both surgical methods can effectively eliminate the lesion and improve the immune function of patients.

Effectively prolonging the postoperative survival time and preventing the recurrence to the largest extent are the ultimate goals of EGC treatment [15]. A number of studies have demonstrated that after EMR and traditional laparotomy, the survival rate is comparable, and the postoperative recurrence rate is 1.9-18.0% and 1.7-3.4%, respectively [16-18]. The follow-up results in this study showed that the survival rate and recurrence rate in the EMR group and the radical surgery group were 95.0% *vs.* 98.3% and 5.0% *vs.* 3.3%, respectively, indicating that the prognosis is good in both groups.

Conclusions

In conclusion, the treatment of EGC with EMR has comparable clinical effect and prognosis to the traditional radical surgery, which causes less damage to the body and gastrointestinal function and less inhibition on the immune function, so it is worthy of clinical application.

Conflict of interests

The authors declare no conflict of interests.

References

1. Kosaka T, Endo M, Toya Y et al. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a single-center retrospective study. Dig Endosc 2014;26:183-91.
2. Balmadrid B, Hwang JH. Endoscopic resection of gastric and esophageal cancer. Gastroenterol Rep (Oxf) 2015;3:330-8.
3. Sugano K. Detection and Management of Early Gastric Cancer. Curr Treat Options Gastroenterol 2015;13:398-408.
4. Chen H, Sui W. Influence of obesity on short- and long-term outcomes after laparoscopic distal gastrectomy for gastric cancer. JBUON 2017;22:417-23.
5. Mocanu A, Barla R, Hoara P, Constantinoiu S. Current endoscopic methods of radical therapy in early esophageal cancer. J Med Life 2015;8:150-6.
6. Tada M. Development of the strip-off biopsy. Gastroenterol Endosc 1984;26:833-9.
7. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1-19.
8. Yin LK, Sun XQ, Mou DZ. Value of Combined Detection of Serum CEA, CA72-4, CA19-9 and TSGF in the Diagnosis of Gastric Cancer. Asian Pac J Cancer Prev 2015;16:3867-70.
9. Monteleone AM, Monteleone P, Serino I, Scognamiglio P, Di Genio M, Maj M. Childhood trauma and cortisol awakening response in symptomatic patients with anorexia nervosa and bulimia nervosa. Int J Eat Disord 2015;48:615-21.
10. Dasopoulou M, Briana DD, Boutsikou T et al. Motilin and gastrin secretion and lipid profile in preterm neonates following prebiotics supplementation: a double-blind randomized controlled study. J Parenter Enteral Nutr 2015;39:359-68.
11. Eren M, Colak O, Isiksoy S, Yavuz A. Effect of H. pylori infection on gastrin, ghrelin, motilin, and gastroesophageal reflux. Turk J Gastroenterol 2015;26:367-72.
12. Katsinelos P, Chatzimavroudis G, Zavos C, Fasoulas K, Katsinelos T, Kountouras J. Volume reduction of a giant pedunculated colonic polyp after endoclipping facilitates endoscopic resection. Surg Laparosc Endosc Percutan Tech 2009;19:e228-e9.
13. Chen SL, Cai SR, Zhang XH et al. Expression of $CD4^+CD25^+$ regulatory T cells and Foxp3 in peripheral blood of patients with gastric carcinoma. J Biol Regul Homeost Agents 2016;30:197-204.
14. Huang XM, Liu XS, Lin XK et al. Role of plasmacytoid dendritic cells and inducible costimulator-positive regulatory T cells in the immunosuppression microenvironment of gastric cancer. Cancer Sci 2014;105:150-8.
15. Ono H, Yao K, Fujishiro M et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Dig Endosc 2016;28:3-15.
16. Choi KS, Jung HY, Choi KD et al. EMR versus gastrectomy for intramucosal gastric cancer: comparison of long-term outcomes. Gastrointest Endosc 2011;73:942-8.
17. Park JC, Lee SK, Seo JH et al. Predictive factors for local recurrence after endoscopic resection for early gastric cancer: long-term clinical outcome in a single-center experience. Surg Endosc 2010;24:2842-9.
18. Chung JW, Jung HY, Choi KD et al. Extended indication of endoscopic resection for mucosal early gastric cancer: analysis of a single center experience. J Gastroenterol Hepatol 2011;26:884-7.