

## Retrospective Study

**Clinical outcomes of Clutch Cutter endoscopic submucosal dissection for older patients with early gastric cancer**

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**Abstract****AIM**

To evaluate the clinical outcome of endoscopic sub-

mucosal dissection using the Clutch Cutter (ESDCC) in older patients.

### METHODS

We reviewed 232 consecutive patients with early gastric cancer who underwent ESDCC between June 2010 and February 2014 at Aso Iizuka Hospital. We divided patients into two groups according to age: Older patients (> 80 years,  $n = 64$ ) and non-older patients ( $\leq 80$  years,  $n = 168$ ). We retrospectively compared the prevalence rates of pre-existing comorbidities, anticoagulant therapy, *en bloc* resection, mean duration of hospitalization, incidence of ESDCC-related complications, change in performance status (PS) before and after ESDCC, and financial cost of admission.

### RESULTS

The older group comprised 64 patients with a mean age of 84.1 years, and the non-older group comprised 168 patients with a mean age of 69.5 years. Older patients had significantly more pre-existing comorbidities than did non-older patients, specifically heart disease ( $P < 0.05$ ). The *en bloc* resection rate in non-older patients was significantly higher than that in older patients (100% vs 95.3%,  $P = 0.02$ ). There were no significant differences between the older and non-older groups in the incidence of ESDCC-related complications (*i.e.*, postoperative bleeding and perforation) and the post-ESDCC change in PS. There were also no significant differences between the older and non-older groups in the mean duration of hospitalization (11.4 and 10.7 d, respectively) and financial cost of admission (657040 JPY and 574890 JPY, respectively).

### CONCLUSION

ESDCC has a good clinical outcome in older patients.

**Key words:** Older patients; Clutch Cutter; Endoscopic submucosal dissection; Early gastric cancer; Financial cost; Duration of hospitalization

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**Core tip:** No previous reports have described the clinical outcomes of endoscopic submucosal dissection using the Clutch Cutter (ESDCC) for older patients with early gastric cancer (EGC). The present study evaluated the clinical outcomes, including medical economics, associated with ESDCC for older patients. There was no significant difference between older patients and non-older patients in the rate of ESDCC-related complications. There was also no significant difference between older and non-older patients in the mean duration of hospitalization and medical economics. We conclude that ESDCC is safe and effective for older and non-older patients with EGC.

Otsuka Y, Akahoshi K, Yasunaga K, Kubokawa M, Gibo J, Osada S, Tokumaru K, Miyamoto K, Sato T, Shiratsuchi Y, Oya M, Koga H, Ihara E, Nakamura K. Clinical outcomes of Clutch Cutter



Figure 1 The distal tip of the Clutch Cutter (long type: Blade length of 5 mm).

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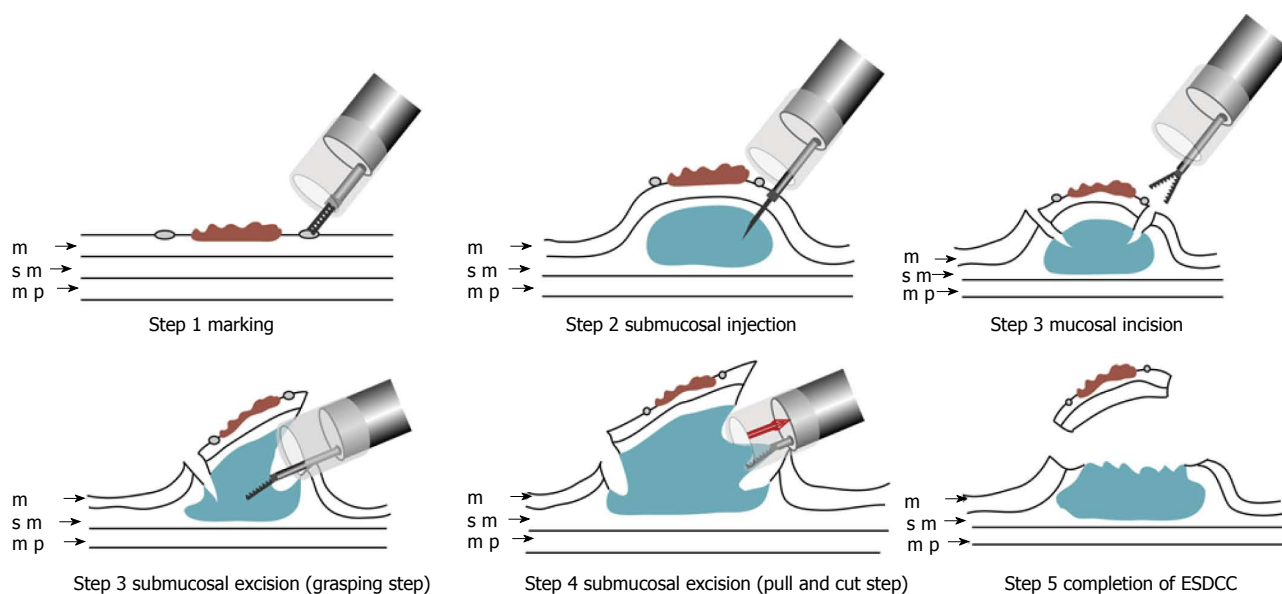
## INTRODUCTION

In an increasingly older society, a growing number of endoscopic treatments are being performed in patients with age-associated comorbidities<sup>[1]</sup>. Endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) has become widely accepted, as it provides *en bloc* resection and histologically complete resection, and it is less invasive than surgical resection<sup>[2-5]</sup>. ESD recently been reported to be a safe and reliable procedure for treating early gastrointestinal tract cancer in older patients<sup>[6-10]</sup>. However, there is little information on the medical costs of ESD, the mean duration of hospitalization, and the change in performance status (PS) before and after ESD. Akahoshi and Fujifilm<sup>[11]</sup> developed a grasping-type scissors forceps [*i.e.*, the "Clutch Cutter" (CC), Fujifilm, Tokyo, Japan, Figure 1] for safe ESD. We previously showed that ESD using the CC (ESDCC) is a safe and effective method for treating patients with early cancer in the esophagus, stomach, duodenum, or colorectum<sup>[11-17]</sup>. However, no reports have described the clinical outcomes of ESDCC for older patients with EGC. The present study evaluated the clinical outcomes of ESDCC for older patients with EGC, including the medical economics associated with ESDCC.

## MATERIALS AND METHODS

### Patients

ESDCC was performed in 269 consecutive patients with EGC between June 2010 and February 2014 at Aso Iizuka Hospital. A total of 37 patients were excluded because their post-ESD histological analysis did not meet the clinical indication criteria for ESD proposed by Gotoda *et al.*<sup>[18]</sup> and the Japanese Gastric Cancer Association<sup>[19]</sup> (*i.e.*, listed in the exclusion criteria group).



**Figure 2** Schema showing endoscopic submucosal dissection using the Clutch Cutter technique. m: Mucosa; sm: Submucosa; mp: Muscularis propria; ESDCC: Endoscopic submucosal dissection using the Clutch Cutter.

A total of 232 consecutive patients with EGC were enrolled in this retrospective study.

We divided the patients into two groups according to age: Older patients (> 80 years, mean age: 84.1 SD ± 3.2 years old) and non-older patients (≤ 80 years, mean age: 69.5 SD ± 7.3 years old). The following factors were retrospectively compared between the two groups: Pre-existing comorbidities, anticoagulant therapy, *en bloc* resection rate, mean duration of hospitalization, incidence of ESDCC-related complications, change in PS before and after ESD, and financial cost of admission. We used a prospectively maintained ESDCC database for the analyses of anticoagulant therapy, *en bloc* resection rate, and incidence of ESDCC-related complications; our institutional medical and accounting records for each patient were used to analyze pre-existing comorbidities, mean duration of hospitalization, change in PS after ESD, and financial cost of admission. PS was classified using the Eastern Cooperative Oncology Group scale. The indication for ESD was a PS score of 0, 1, or 2.

### ESD with the Clutch Cutter procedure

Detailed technical procedures of ESDCC have been reported previously<sup>[11-17]</sup> (Figure 2). ESDCC was conducted using a single-channel therapeutic endoscope (EG-450RD5; Fujifilm) or a two-channel multi-bending endoscope (GIF-2T240M; Olympus, Tokyo, Japan). A long, transparent hood (F-01; Top Co. Ltd., Tokyo, Japan) was attached to the tip of the endoscope to facilitate submucosal dissection by elevating the lesion. Circumferential markings were made using the CC in closed mode. A hyaluronic acid solution (MucoUp; Johnson and Johnson, Tokyo, Japan) with diluted epinephrine (0.0002%) and indigo carmine (0.0002%) was injected into the submucosal layer to lift up the lesion. The target mucosal and submucosal layer tissues

were grasped, lifted up, and cut using the CC. Finally, the lesion was completely resected using the CC (Figure 3). When bleeding occurred during the procedure, it was treated *via* coagulation with the CC. The forced coagulation mode (VIO 300D; Erbe, Tübingen, Germany) 30 W (effect 3) was used for marking, the endo cut Q mode (effect 2, duration 3, interval 1) was used for cutting, and the soft coagulation mode 100 W (effect 5) was used for hemostatic treatment.

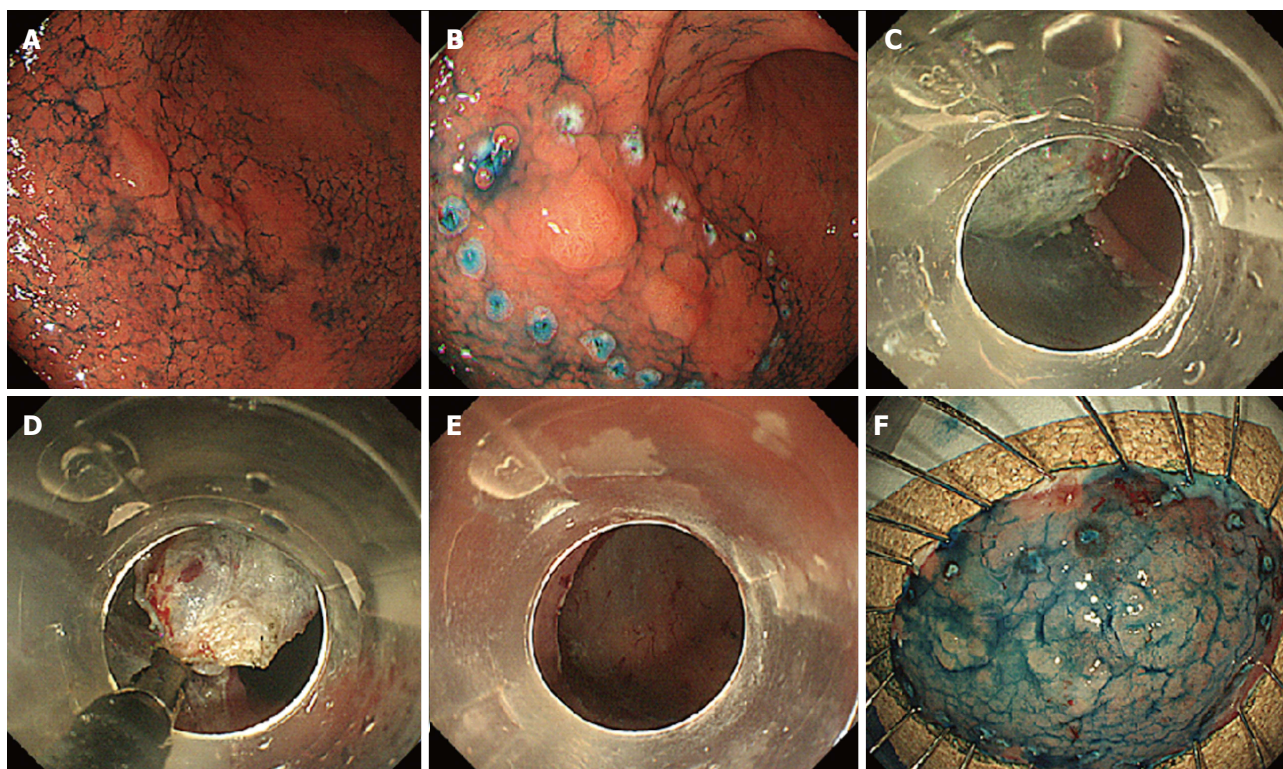
### Statistical analysis

Statistical analyses for comparison between the older and non-older groups was performed using the  $\chi^2$ -test, the Wilcoxon/Kruskal-Wallis test, and Fisher's exact probability test. The  $\chi^2$ -test was used to evaluate intergroup differences in anticoagulant therapy and *en bloc* resection, incidence of ESDCC-related complications, and change in PS before and after ESD. The Wilcoxon/Kruskal-Wallis test was used to evaluate intergroup differences in the mean duration of hospitalization and financial cost of admission. Fisher's exact probability test was used to evaluate intergroup differences in pre-existing comorbidities. Differences were considered significant at  $P < 0.05$ .

## RESULTS

### Patients' characteristics

The older group comprised 64 patients with a mean age of 84.1 years, and the non-older group comprised 168 patients with a mean age of 69.5 years (Table 1). The two groups significantly differed in terms of age, but not sex. Older patients had a significantly higher rate of pre-existing comorbidities than did non-older patients ( $P < 0.05$ ), especially heart disease. The proportion of the older group receiving anticoagulant therapy was not



**Figure 3** Endoscopic submucosal dissection using the Clutch Cutter in an 82-year-old Japanese male. A: Indigo carmine was sprayed to demarcate the lesion; B: Markings outside the lesion; C and D: The submucosal tissue under the lesion was gradually grasped and dissected from the muscle layer; E: The lesion was completely cut from the muscle layer; F: Fixation of the specimen.

**Table 1** Patient characteristics *n* (%)

	Older group ( <i>n</i> = 64)	Non-older group ( <i>n</i> = 168)	<i>P</i> value
Mean age	84.2	69.5	
Gender ratio (M/F)	44/20	118/50	NS
No. of performance state 3 or 4	5 (7.8)	4 (2.4)	
Pre-existing comorbidity			
Total prevalence rates	58 (90.6)	123 (73.2)	0.0042
Cerebral infarction	11 (17.2)	17 (10.1)	NS
Cardiovascular disease	23 (35.9)	25 (14.9)	0.0004
Respiratory disease	8 (12.5)	12 (7.1)	NS
Chronic renal dysfunction	8 (12.5)	21 (12.5)	NS
Liver cirrhosis	1 (1.6)	12 (7.1)	NS
Diabetes	20 (31.2)	47 (28.0)	NS
Hypertension	44 (68.8)	98 (58.3)	NS
Senile dementia	7 (10.9)	14 (8.3)	NS
Anti-coagulant therapy	4 (6.3)	12 (7.1)	NS

NS: Not significant.

significantly different to that of the non-older group.

### Tumor characteristics

No significant between-group differences were found regarding the macroscopic type, tumor size, histological type, and ESD indication categories (Table 2). However, the proportion of upper lesions was significantly higher in the older group (43.8%) than in the non-older group (23.2%) ( $P = 0.0042$ ).

**Table 2** Tumors characteristics

	Older group ( <i>n</i> = 64)	Non-older group ( <i>n</i> = 168)	<i>P</i> value
Location			
Upper	28	39	0.019
Middle	16	55	NS
Lower	20	72	NS
Residual stomach	0	2	
Mean tumor size	17.5	15.6	NS
Histological type			
Well differentiated	58	149	NS
Moderately differentiated	5	10	NS
Poorly differentiated	0	8	NS
Papillary differentiated	1	1	NS
Category of indication			
Guideline lesion	47	118	NS
Lesion included in the expanded indications	17	50	NS

NS: Not significant.

### Technical outcomes

The R0 resection rate in the non-older group was significantly higher than that in the older group (100% vs 95.3%,  $P = 0.02$ , Table 3). However, the R0 resection rate was greater than 95% in both groups. The postoperative bleeding rates of the older and non-older groups were 1.6% (1/64) and 4.8% (8/168), respectively. Perforation occurred in only one (1.6%) patient in the older group; endoscopic clipping was performed in this patient and the

**Table 3** Technical outcome *n* (%)

	Older group ( <i>n</i> = 64)	Non-older group ( <i>n</i> = 168)	<i>P</i> value
<i>En bloc</i> resection	63 (98.4)	168 (100)	NS
R0 resection	61 (95.3)	168 (100)	0.03
Complications			
Intraoperative hemorrhage	0 (0)	0 (0)	NS
Intraoperative perforation	1 (1.6)	0 (0)	NS
Postoperative hemorrhage	1 (1.6)	8 (4.8)	NS
Postoperative perforation	0 (0)	0 (0)	NS

NS: Not significant.

perforation was cured. There was no significant difference between the two groups in the rate of ESDCC-related complications.

### Social and economic outcomes

Three patients in the older group and one patient in the non-older group showed a worse PS after ESD, but there was no significant difference between groups in the prevalence of a worse PS after ESD. The mean duration of hospitalization in the older and non-older groups was 11.4 and 10.7 d, respectively. The mean financial costs of admission for the older and non-older groups were 657040 JPY and 574890 JPY, respectively. There were no significant differences between the two groups in duration of hospitalization or admission costs (Table 4).

## DISCUSSION

According to the 2014 fiscal statistics published by the Ministry of Health, Labour and Welfare, the life expectancies of men and women are 80.5 years old and 86.8 years old, respectively<sup>[20]</sup>. The natural history of EGC is unclear. However, a long life expectancy and an aging population will inevitably lead to an increased number of older patients with EGC in Japan. Long-term outcomes suggest that implementation of ESD for older patients with a satisfactory PS will increase life expectancy<sup>[21]</sup>. Therefore, we investigated the clinical outcomes associated with older patients who received ESDCC for EGC, including economic and social aspects.

As expected, older patients in our study had significantly more pre-existing comorbidities than did non-older patients. In our study, the rate of pre-existing comorbidities was higher than that in previous reports because the mean age of our patients was older than that in previous reports<sup>[8,22]</sup>. Tokioka *et al.*<sup>[8]</sup> and Chinda *et al.*<sup>[22]</sup> reported that older patients were more likely to receive anticoagulant therapy than non-older patients. However, the proportions of older and non-older patients in our study who received anticoagulant therapy were almost equal. The current study included five (7.8%) and four (2.4%) patients who had PSs of 3 and 4 in the older group and the non-older group, respectively,

**Table 4** Social and economic outcomes *n* (%)

Parameter	Older group ( <i>n</i> = 64)	Non-older group ( <i>n</i> = 168)	<i>P</i> value
Worsening of the performance status	3/64 (4.7)	1/168 (0.6)	NS
Mean duration of hospitalization (d)	11.4	10.7	NS
Mean financial cost of admission (JPY)	657040	574890	NS

NS: Not significant.

as they strongly desired treatment. The PSs of these patients did not change after the procedure. However, three (4.7%) patients in the older group and one (0.6%) patient with senile dementia in the non-older group showed a worse PS after ESD. Three patients in the older group had several pre-existing comorbidities. Although ESD is less invasive than an operation, care should be taken regarding patients with several pre-existing comorbidities.

No significant between-group differences were observed regarding macroscopic type, tumor size, histological type, and ESD indication categories. ESD was performed on the lesions of these patients, similar to a previous report<sup>[8]</sup>. In our study, the proportion of upper lesions was significantly higher in the older group than in the non-older group. Furthermore, the R0 resection rate in the non-older group was significantly higher than that in the older group. The tumor location likely affects the difficulty of the ESD procedure, and so the greater number of upper lesions in older patients might have affected the technical outcomes.

The current study did not show a significant difference between older and non-older patients in the rate of ESDCC-related complications (*i.e.*, postoperative bleeding and perforation). The reported perforation and bleeding rates of ESD using a knife device range from 1.2% to 8.2% and from 5.3% to 15.6%, respectively<sup>[23-30]</sup>. Our complication rate was low compared with that reported in previous studies that used conventional knives<sup>[23-30]</sup>. Inevitable risk factors associated with knife devices for ESD-related complications include defects of fixation (inaccurate targeting) and compression (hemostatic effect), as well as pushing the knife into the target tissue (where the pushing force is in the direction of the muscle layer) with an electric discharge<sup>[14]</sup>. The CC can accurately grasp target tissue and can be energized or incised while separated from the muscular layer, thus greatly reducing the risks. There was no uncontrollable intraoperative bleeding in our previous reports on ESD<sup>[11-17]</sup>. We were able to quickly and easily stop intraoperative bleeding using the CC<sup>[15]</sup> without changing the device for the entire gastrointestinal tract. In the present study, we did not perform any unexpected incisions. Therefore, the CC has the potential to decrease the risk of ESD-related complications in older and non-older patients.

Our study found no significant difference between older and non-older patients in the mean duration of hospitalization. Tokioka *et al.*<sup>[8]</sup> also failed to find a significant difference in the mean duration of hospitalization between these two groups (13.3 d vs 10.3 d). However, these authors reported that older patients with complications due to ESD (*i.e.*, perforation) were hospitalized for significantly longer periods than non-older patients<sup>[8]</sup>. In our series, we encountered perforation in one older patient who underwent endoscopic clipping and required 16 d of hospitalization. Therefore, preventing complications, such as perforation, is important for reducing the duration of hospitalization, especially in older patients.

Few medical economic outcomes have been reported in older patients. Murata *et al.*<sup>[31]</sup> reported that mean medical costs are significantly higher for older patients undergoing ESD for EGC than for non-older patients. They also reported that chronic comorbid conditions or the use of anticoagulant drugs, as well as the occurrence of complications, might be associated with an increase in the length of stay or medical costs during hospitalization<sup>[31]</sup>. Although the older group in our study showed a significantly higher rate of comorbid cardiovascular disease than did the non-older group, the postoperative bleeding rate was low in the older group (1.6%). In our series, there were no significant between-group differences in the length of stay and medical costs during hospitalization. The reported complication rate associated with ESDCC is lower than that of ESD using conventional knives<sup>[11-17]</sup>, which might have affected our medical economic outcomes.

We conclude that ESDCC is safe and effective for older and non-older patients with EGC. This study is limited by its retrospective nature. A prospective study with a larger sample size is advised.

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We thank Kelly Zammit, BVSc, for editing a draft of this manuscript. Kazuya Akahoshi and Hidefumi Akahane (Fujifilm) have applied for a patent in Europe for the CC described in this article. Japan, China, and the United States have already granted patents.

## COMMENTS

### Background

In an aging society, the opportunity to treat older patients with early gastric cancer (EGC) is increasing. However, there is little information on the medical costs of endoscopic submucosal dissection (ESD), the mean duration of hospitalization, and the change in performance status before and after ESD. It is important to assess the clinical outcomes of ESD using the Clutch Cutter (CC) (ESDCC) in older patients with EGC.

### Research frontiers

The authors previously showed that ESD using the CC (ESDCC) is a safe and effective method for treating patients with early cancer in the gastrointestinal tract. No reports have yet evaluated the efficacy and safety of ESDCC for older patients with EGC, including the economic and social aspects.

## Innovations and breakthroughs

There was no significant difference between older patients and non-older patients in mean duration of hospitalization, incidence of ESDCC-related complications, change in PS before and after ESD, and financial cost of admission.

## Application

It may be economically and socially beneficial to reduce the complication rate by performing ESDCC for older patients with EGC.

## Terminology

The CC (DP2618DT, Fujifilm Corporation, Tokyo, Japan) was developed by Akahoshi. The CC is a grasping type of scissors/forceps that can grasp tissue pieces and cut or coagulate with an electrosurgical current. To facilitate tissue grasping, the CC has a serrated cutting edge with a width of 0.4 mm, and a length of 3.5 mm or 5 mm. The forceps diameter is 2.7 mm. The outside of the forceps is insulated so that electrosurgical current energy concentrates on the closure blade to avoid unintentional incision. Furthermore, the forceps can be rotated in any desired direction. The CC is disposable and cannot be reused. The CC can be used in all steps of ESD.

## Peer-review

The authors present an interesting study on the efficacy and safety of endoscopic submucosal dissection for older patients with early gastric cancer. The study is well designed, the results are accurately noted and the discussion is concise.

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