Clinical Results Following Colonic Resection for Ulcerative Colitis in Elderly Individuals (Elderly-onset Versus Nonelderly Onset)

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Abstract

Background

The incidence of ulcerative colitis (UC) is increasing, but there are few reports comparing elderly UC patients undergoing colectomy for elderly-onset UC (EOUC) and nonelderly-onset UC (NEOUC). The aim of this study was to analyze the differences between EOUC and NEOUC patients who underwent UC-related surgery.

Methods

We identified 1973 patients with UC who underwent colectomy at Hyogo College of Medicine between January 1, 1984, and December 31, 2018. Only patients aged 65 years old and older who underwent colectomy were enrolled in this study (n=221, 11.2%), and their clinical records were retrospectively reviewed. Patients were divided into two groups according to their age at disease onset: those with onset at younger than 60 years old (NEOUC) and at 60 years old or older (EOUC).

Results

In the 221 UC patients who underwent colectomy at 65 years old or older, there were 155 cases of EOUC and 66 cases of NEOUC. The main surgical indication in NEOUC patients was colitis-associated cancer/dysplasia (32/66, 47%). In contrast, refractory to medical treatment was the leading cause of surgery in EOUC patients (80/155, 52%). The distributions of surgical indications were different between the two groups ($p<0.01$).

The preoperative daily dose of steroids was significantly higher in the EOUC group than in the NEOUC group (0 mg vs 10 mg, $p<0.01$). The rates of immunosuppressant, infliximab (IFX) and adalimumab use did not differ significantly between the groups. Significantly more patients underwent emergency surgery in the EOUC group than in the NEOUC group (14% vs 35%, $p<0.01$).

The proportions of patients with postoperative morbidity (Clavien-Dindo grade III or higher) were 17.4% (27/155) in the EOUC group and 13.6% (9/66) in the NEOUC group. There was no significant difference between the two groups ($p=0.48$). The prognosis of the EOUC patients who underwent UC-related emergency surgery was worse than that of the NEOUC patients ($p<0.01$). In the EOUC group, 8 (14.8 %) of 54 patients died within 30 postoperative days, while there were no deaths in the NEOUC group.

Conclusion

Among elderly UC patients undergoing UC-related surgery, EOUC patients undergoing emergency surgery had very poor outcomes, and the mortality rate was 14.8%. In such cases, it is important for physicians and surgeons to begin communication at an early stage so that the optimal surgical timeframe is not missed.

Background

Ulcerative colitis (UC) is a refractory disease with an unknown cause. While considered a condition primarily affecting young adults, UC can develop at any age, including old age. In fact, UC has bimodal incidence peaks, with the second peak occurring between the ages of 50-80 years. [**1-6**]

Elderly patients with US can be divided into two groups: those with elderly-onset UC (EOUC) and those with nonelderly-onset UC (NEOUC). The largest population-based study evaluating the natural history of EOUC was performed in France and reported a milder disease course in elderly-onset irritable bowel disease (IBD) patients compared with pediatric and adult-onset IBD patients. [**7**] However, EOUC has also been reported in other studies as a predictive factor for increased morbidity and mortality [**8.9**].

According to recent Japanese nationwide survey data, attention has been focused on the increasing number of EOUC cases. Komoto et al. [**10**] reported that EOUC patients show increased disease activity, with an increased proportion requiring UC-related hospitalization and UC-related surgery. Over the last decade, several new therapies for UC (immunosuppressors, biologics) have improved patient outcomes, and these treatments are included in international guidelines. [**11.12**] Therefore many NEOUC patients avoid colectomy. However, as patients grow older, the need for colectomy increases due to colitis-associated colorectal cancer/dysplasia.

Thus, colectomy for UC in elderly patients is increasing [**13**], but there are few reports about elderly UC patients who underwent colectomy. There is no study comparing EOUC and NEOUC. The aim of this study was to analyze the differences in patient characteristics, preoperative medical treatment, surgical indications, and short-term outcomes, especially postoperative mortality, between EOUC and NEOUC patients aged 65 years and older who underwent UC-related surgery.

Methods

(Inclusion and exclusion criteria)

We identified 1973 patients with UC who underwent colectomy at Hyogo College of Medicine between January 1, 1984, and December 31, 2018. Only the data of patients who were 65 years old and older and underwent colectomy were retrospectively analyzed in this study (n=221, 11.2%).

(Research methods)

Patients were divided into two groups according to their age at disease onset: those younger than 60 years old (NEOUC) and those 60 years old and older (EOUC). The following data were retrospectively collected: age at surgery, sex, severity, preoperative medication, surgical indications, emergency surgery, postoperative complications (Clavien-Dindo classification grade ≦III), and mortality. In this study, we compared these data between the two groups.

(Definitions)

Acute severe colitis was defined according to Truelove and Witt's criteria. [14]

Surgery was determined as ‘elective’ if the decision to operate for UC was made prior to hospital admission, whereas the decision to perform ‘emergency’ colectomy was decided during or after admission on the basis of acute complications or for UC refractory to in-hospital intensive medical management.

Early postoperative complications were classified into 5 severity grades according to Dindo et al. [15] In this study, postoperative complications occurred within 30 days after surgery and were classified as Clavien-Dindo grade III or higher. Postoperative mortality was defined as death related to the surgical procedure during the first 30 postoperative days.

(Statistical analysis)

All statistical analyses were carried out using JMP ver. 12 (SAS Institute, Inc., Cary, North Carolina, USA). Qualitative variables are expressed as frequencies and percentages. Quantitative variables are expressed as medians and ranges. The comparison of quantitative variables was performed by the Mann-Whitney test. For qualitative variables, we used chi-square or Fisher's exact tests. A value of $p < 0.05$ was considered statistically significant.

(Ethical considerations)

Ethical approval for this study was granted by the Institutional Review Board of the Hyogo College of Medicine (No. 202006-038). Each participating patient provided informed consent for participation in the clinical trial.

Results

(Patient backgrounds)

The data of 221 patients who underwent colectomy 65 years old and older were retrospectively analyzed. Among them, 155 patients had EOUC, and 66 patients had NEOUC. Table 1 summarizes the characteristics of the elderly patients in this study. Sex and body mass index were not significantly different between the two groups, although the duration of disease was significantly shorter in the EOUC group than in the NEOUC group (245 months vs 22 months, $p<0.01$). There was no significant difference in the extent of colitis between the two groups, but the incidence of severe or fulminant type UC was significantly greater in the EOUC group than in the NEOUC group ($p<0.01$).

(Preoperative medication)

Preoperative medications are shown in Table 2. The preoperative total dose of steroids was significantly higher in the NEOUC group than in the EOUC group (8250 mg vs 2634 mg, $p<0.01$). In contrast, the preoperative daily dose of steroids was significantly higher in the EOUC group than in the NEOUC group (0 mg vs 10 mg, $p<0.01$). The rates of immunosuppressant, infliximab (IFX) and adalimumab use did not differ significantly between the groups. EOUC patients underwent cytapheresis much more frequently than NEOUC patients (24.2% vs 38.7%, $p=0.04$).

(Surgical indications)

The surgical parameters are shown in Table 3. The main surgical indication in NEOUC patients was colitis-associated cancer/dysplasia (32/66, 47%). In contrast, refractory medical treatment was the leading cause of surgery in EOUC patients (80/155, 52%). The distribution of surgical indications was different between the two groups ($p<0.01$). Significantly more patients underwent emergency surgery in the EOUC group than in the NEOUC group (14% vs 35%, $p<0.01$).

(Postoperative complications)

Table 4 shows postoperative complications. The postoperative morbidity (Clavien-Dindo grade III or higher) was 17.4% (27/155) in the EOUC group and 13.6% (9/66) in the NEOUC group. There was no significant difference between the two groups. The most common postoperative complications were intrabdominal abscess in NEOUC patients and pneumonia in EOUC patients. In the EOUC group, there were 2 cases of residual rectum bleeding and 2 cases of duodenum bleeding. Other sources of bleeding were tumors and the inferior epigastric artery.

(Postoperative mortality)

Postoperative mortality within 30 postoperative days was 5.8% (9/155) in the EOUC group and 1.5% (1/66) in the NEOUC group. (Table 5) There were no significant differences between the two groups ($p=0.29$). Additionally, we examined the mortality rate considering emergency or elective surgery. In elective cases, there were no significant differences between the two groups ($p=0.57$). However, in the emergency setting, there were significant differences ($p<0.01$). The prognosis of EOUC patients who underwent emergency surgery was extremely poor, and the mortality rate was 14.8% (8/54) (Table 6).

The leading cause of postoperative death in EOUC patients who underwent emergency surgery was pneumonia (11.1%, 6/54). Sepsis caused by leakage from the stump following the Hartmann procedure and bleeding of the inferior epigastric artery were other causes of death.

Discussion

It is well known that UC has a bimodal incidence distribution[**1-6**] Especially in recent years, the rate of UC in elderly individuals has increased[**16**]**.** There are various reports on UC in elderly individuals. It was once reported that the disease course in elderly UC patients was relatively mild[**17.18**]**.** However, the number of UC-related surgery cases in elderly individuals is increasing. Recently, it has been shown that elderly UC patients can be classified into two groups with different characteristics: those with EOUC and with NEOUC10. Therefore, we compared these two groups in elderly UC patients who underwent surgery.

Regarding postoperative complications (Clavien-Dindo grade III or higher), there was no significant difference between the EOUC and NEOUC groups. Among the postoperative complications, infection accounted for 55% (5/9) in the NEOUC group and 66% (18/27) in the EOUC group. Preoperative steroid therapy has been reported to increase the risk postoperative infection[**10**], and preoperative medical treatment may have an impact on infection. Regarding perioperative mortality, there was no significant difference between the two groups among those who underwent elective surgery ($p=0.57$). Among those who required emergency surgery, EOUC patients had a very high mortality rate of 14.5%, which was significantly different from that in NEOUC patients ($p<0.01$). Increased mortality due to UC-related emergency surgery in elderly patients has previously been reported[**19**], but there were no reports comparing NEOUC and EOUC cases.

The most common cause of death was pneumonia. Accordingly, it is considered necessary to evaluate the preoperative respiratory system. Cautious treatment selection and moderate surgical intervention may be needed for patients with respiratory disease or a high risk of perioperative pneumonia.

In Japan, the early and aggressive administration of immunosuppressants was started in the early 2000s. Tacrolimus (Tac) and biological therapies have been covered by insurance since 2009 and 2010, respectively. Especially in Japan, Tac and IFX are often used to induce remission of severe UC. In recent years, progress in the medical treatment of UC has been remarkable. With the advent of new drugs, medical treatment options are increasing. In fact, there are also new gut-targeted biologics, such as vedolizumab, which may have a more favorable safety profile and shift decision making toward medical therapy [**20**]**.**

Although there are many cases in which young people may require second-line and third-line therapies, considering the prognosis of EOUC patients in this study, it is important to treat EOUC cases carefully so that emergency surgery can be avoided; it is important to recognize the appropriate timing for the transition to surgical treatment and not miss the optimal treatment window. In other words, in the case of EOUC, it is necessary to make a strict judgment regarding medical treatment not prolong the decision longer than necessary. In addition, physicians and surgeons should collaborate to treat EOUC patients to avoid errors in the timing of surgery. When surgery is deemed appropriate, performing surgery under elective conditions rather than under emergent conditions can substantially reduce mortality.

We previously reported that an Onodera’s prognostic nutritional index

(10 × serum albumin (g/dL) + 0.005 × total lymphocyte count) [21] of 25 or less is a risk of postoperative mortality in UC patients and that the mortality rate was 13.6% (6/44) [22]. This index may be a useful indicator of surgery timing.

This study has some limitations. First, this was a retrospective study. Second, our facility is an IBD-specialty hospital, and the patient population may be different from that in the real world. Third, old data were included in this study, and there were missing data on the underlying diseases of patients; thus, it was not possible to evaluate these.

Conclusion

Among UC elderly patients who underwent UC-related surgery, the outcomes of emergency surgery in EOUC patients were very poor compared with those in NEOUC patients; the mortality rate was 14.8%. The most common cause of death was pneumonia.

In such cases, it is important for the physician and surgeon to begin communication at an early stage so that the optimal timeframe for surgery is not missed.

Abbreviations

UC : ulcerative colitis

EOUC : elderly-onset UC

NEOUC : nonelderly-onset UC

Tac : Tacrolimus

Declarations

Ethics approval and consent to participate

Ethical approval for this study was granted by the Institutional Review Board of the Hyogo College of Medicine (No. 202006-038). Because this was retrospective study, consent for participation was opt-out.

Consent for publication

Not Applicable

Coppeting interest

The authors have no conflicts of interest to declare.

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Tables

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