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Retrospective Study

Emergency exploratory laparotomy and radical gastrectomy in patients with gastric

cancer combined with acute upper gastrointestinal bleeding

Kuang F et al. GC patients combined with acute UGIB

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Abstract

BACKGROUND

Gastric cancer (GC) is a prevalent malignant tumor worldwide and ranks as the fourth

leading cause of cancer-related mortality. Upper gastrointestinal bleeding (UGIB) is a

frequent complication of GC. Radical gastrectomy and palliative therapy are widely

used surgical procedures in the clinical management of GC. This study intends to probe

the clinical efficacy and safety of radical gastrectomy and palliative therapy on the basis of exploratory laparotomy in patients with GC combined with UGIB, hoping to provide

valuable information to aid patients in selecting the appropriate surgical intervention.

AIM

To investigate the clinical efficacy and safety of exploratory laparotomy + radical

gastrectomy and palliative therapy in patients with GC and UGIB combined.

METHODS

A total of 89 GC patients admitted to The First Affiliated Hospital of the University of

South China between July 2018 and July 2020 were selected as participants for this

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study. The 89 patients were divided into two groups: radical resection group (*n* = 46) treated with exploratory laparotomy + radical gastrectomy and Palliative group (*n* = 43) treated with palliative therapy. The study compared several variables between the two groups, including surgical duration, intraoperative blood transfusion volume, postoperative anal exhaust time, off-bed activity time, length of hospitalization, and incidence of complications such as duodenal stump rupture, anastomotic obstruction, and postoperative incision. Additionally, postoperative immune function indicators (including CD3+, CD4+, CD8+, CD4+/CD8+, and CD3+/HLADR+), immunoglobulin (IgG and IgM), tumor markers (CEA, CA199, and CA125), and inflammatory factors (IL-6, IL-17, and TNF-α) were assessed. The surgical efficacy and postoperative quality of life recovery were also evaluated. The patients were monitored for survival and tumor recurrence at 6 mo, 1 year, and 2 years post-surgery.

RESULTS

The results indicated that the duration of operation time and postoperative hospitalization did not differ between the two surgical procedures. However, patients in the radical resection group exhibited shorter intraoperative blood loss, anus exhaust time, off-bed activity time, and inpatient activity time than those in the Palliative group. Although there was no substantial difference in the occurrence of postoperative complications, such as duodenal stump rupture and anastomotic obstruction, between the radical resection group and Palliative group (P > 0.05), the radical resection group exhibited higher postoperative immune function indicators (including CD3+, CD4+, CD8+, etc.) and immunoglobulin levels (IgG, IgM) than the Palliative group, while tumor markers and inflammatory factors levels were lower than those in the radical resection group. Additionally, surgical efficacy, postoperative quality of life, and postoperative survival rates were higher in patients who underwent radical gastrectomy than in those who underwent palliative therapy. Moreover, the probability of postoperative tumor recurrence was lower in the radical gastrectomy group

compared to the palliative therapy group, and these differences were all statistically significant (P < 0.05).

CONCLUSION

Compared to palliative therapy, exploratory laparotomy + radical gastrectomy can improve immune function, reduce the levels of tumor markers and inflammatory factors, improve surgical efficacy, promote postoperative quality of life recovery, enhance survival rates, and attenuate the probability of tumor recurrence.

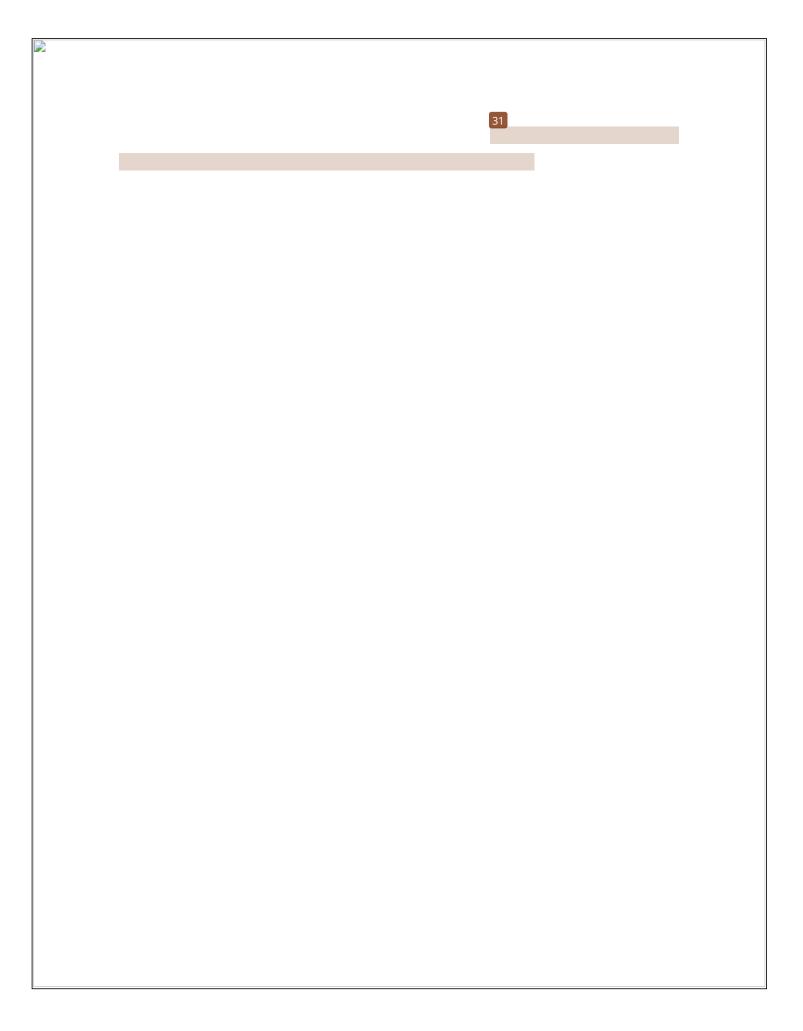
Key Words: Gastric cancer; Exploratory laparotomy; Radical gastrectomy; Upper gastrointestinal bleeding; Safety

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Core Tip: Gastric cancer (GC) is a prevalent digestive system malignancy that commonly results in upper gastrointestinal bleeding (UGIB). Surgery is the primary treatment modality for GC. Radical gastrectomy and palliative therapy are commonly adopted surgical procedures. This present study investigated the clinical efficacy and safety of palliative therapy and exploratory laparotomy + radical gastrectomy in patients with GC and acute UGIB. The outcomes of the study showed that exploratory laparotomy + radical gastrectomy improved surgical efficacy, enhanced survival rates, lowered the probability of tumor recurrence, and bettered the prognosis of patients.

INTRODUCTION

Gastric cancer (GC) is a prevalent malignant tumor of the digestive system and ranks as the fourth leading cause of cancer-related death^[1]. The most common histological type of GC is gastric adenocarcinoma, which is classified into papillary adenocarcinoma,



appropriate and reasonable surgical procedure for GC patients, particularly those with complications.

This retrospective study analyzed the clinical data of 89 GC patients at the hospital to explore the efficacy and safety of palliative therapy and radical gastrectomy in treating patients with GC and acute UGIB on the basis of exploratory laparotomy, in the hope of providing valuable insights for treating GC patients.

MATERIALS AND METHODS

General information

The study subjects comprised 89 patients with GC who were admitted to The First Affiliated Hospital of the University of South China between July 2018 and July 2020. The Ethics Committee of The First Affiliated Hospital of the University of South China approved this study. The 89 patients with GC were divided into two groups based on the surgical methods used: the radical resection group underwent radical gastrectomy (n = 46), while the palliative group received palliative therapy (n = 43). No significant differences were found in the general characteristics of the patients (P > 0.05), indicating comparability (see Table 1).

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) Patients diagnosed with GC via pathological biopsy; (2) Patients without other serious diseases; (3) Patients without mental disorders; (4) Patients with surgical indications, including the absence of severe cardiopulmonary dysfunction or coagulation disorders, tolerance to anesthesia and surgical conditions, and feasibility of surgical treatment confirmed by imaging evaluation; and (5) Patients with upper gastrointestinal bleeding.

Exclusion criteria: (1) Patients with other serious diseases; and (2) Patients with serious mental diseases or communication disorders.

Method

Upon admission, patients in both groups underwent thorough preoperative preparation for standard care. Patients in the palliative group undergoing palliative therapy were initially positioned supine and provided with general anesthesia. A midline incision was made on the upper abdomen, followed by an exploratory laparotomy to assess the location, size, and metastasis of the tumor. Based on the specific condition of each patient, they were then subjected to resection surgery (*e.g.*, proximal gastrectomy, distal gastrectomy, *etc.*) or non-resection surgery^[17].

Patients in the radical resection group underwent radical gastrectomy, using the same anesthesia and exploratory laparotomy techniques as the palliative group. The posterior peritoneum was incised from the lateral side of the patient's duodenum, and D2 lymphadenectomy was used to dissect their lymph nodes. Following dissection, patients received a specific surgical intervention depending on their condition: total gastrectomy for lesions larger than 4 cm, proximal gastrectomy for patients with gastric body and cardia tumors, cardia ulcers with bleeding, perforation or portal hypertension resulting in esophageal variceal rupture and bleeding at the bottom of the stomach; or distal gastrectomy for patients with GC and massive serosal invasion, tumor diameter larger than 10 cm, or lymph node metastases fused and surrounded important blood vessels or extensively infiltrated surrounding tissues^[18].

Observational indicators

Observation and recording of the patient's operation time, intraoperative blood transfusion volume, postoperative hospitalization duration, and other indicators in the two groups: Gastrointestinal metastasis and bleeding are common in patients with GC, and surgeries for these patients often take a long time. In cases where intraoperative bleeding exceeds 1000 mL, patients may experience a significant reduction in vital signs, necessitating timely blood transfusions. Operation time was defined as the period between the beginning of exploratory laparotomy and the end of surgery. The volume of blood transfused throughout the operation was also recorded.

Postoperative hospitalization duration was defined as the time from postoperative

transfer to the ward to the patient's rehabilitation and discharge from the hospital and was measured alongside off-bed activity and anal exhaust time.

Observation and recording of the patient's overall incidence rate of postoperative complications in the two groups: Postoperative complications of GC are primarily associated with patients' physical conditions and surgical procedures^[7,19]. These complications include postoperative bleeding, which is typically characterized by the drainage of small amounts of dark red or brown gastric fluid after surgery, duodenal stump rupture that manifests as acute and severe pain with peritoneal irritation in the right upper abdomen, and anastomotic obstruction, which presents as vomiting after meals or bile-free vomiting. Other possible complications following GC surgery encompass intestinal obstruction, abdominal effusion, reflux gastritis, incision infection, and bleeding. All the postoperative complications were observed, recorded, and divided by the total case numbers to obtain the overall incidence rate of complications.

Observation of the patient's postoperative immune function indicators: We collected 4 mL of venous blood from patients in the two groups 12 wk before and after the surgery. CD3+, CD4+, CD8+, CD4+/CD8+, and CD3+/HLADR+ were detected through flow cytometry, Epics. XLII flow cytometry was harnessed for the assay, the parameters of flow cytometry were set, a 15mW fluoride laser with 488 nm long was adopted as the excitation light source, immunofluorescence data were analyzed *via* Exp032 ADC, and DNA cell cycle was fitted and analyzed by Muticycle AV software. In addition, immunoglobulin (IgG, IgM) levels were gauged using immunonephelometry.

Observation of the patient's levels of tumor markers and inflammatory factors after the operation: Fasting venous blood (3 mL) was harvested 12 wk before and after surgery from patients in the two groups. Serum was separated and analyzed for levels of carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), and carbohydrate antigen 125 (CA125) using chemiluminescence. Additionally, IL-6, IL-17,

and TNF- α were detected *via* enzyme-linked immunosorbent assay, in strict adherence to the manufacturer's instructions^[5,20].

Observation of the patient's surgical efficacy and postoperative quality of life recovery in the two groups: Efficacy was evaluated 6 mo following surgery employing the RECIST1.1 Response Evaluation Criteria in Solid Tumors^[21]. Complete response (CR) was defined as the complete disappearance of all lesions for at least 4 wk. Partial response (PR) refers to a reduction of lesion size by more than 30% and lasting for at least 4 wk. Stable disease (SD) represents a reduction in lesion size of less than 30% or an increase in size of up to 20%. Progressive disease (PD) was defined as a 20% or creater increase in the size of one or more lesions or the appearance of new lesions. Objective response rate (ORR) = (CR + PR)/number of patients in this group × 100%, disease control rate (DCR) = (CR + PR + SD)/number of patients in this group × 100%.

KPS scoring criteria^[22,23] were exploited to evaluate the patient's quality of life after surgery. Improvement was defined as an increase in score by more than 10 points after treatment compared to the score before treatment. Stability was regarded as a change in score of no more than 10 points after treatment, and ineffectiveness as a decrease in score by more than 10 points after treatment. Based on the score, patients' quality of life was classified into one of three categories: improvement, stability, or ineffectiveness, to determine the recovery rate of their quality of life.

Observation of the patient's survival rate and tumor recurrence probability at 6 mo, 1 year and 2 years after the operation: The survival rate and probability of tumor recurrence for patients were monitored at 6, 12, and 24 mo for the purpose of the overall comprehension and tracking of the patient's disease recovery. The postoperative survival rate and tumor recurrence rate were observed and analyzed.

Statistical analysis

The data for this study were processed and analyzed using SPSS 21.0 software. The measurement data were presented as mean \pm SD, and group comparisons were performed using the *t*-test. Enumeration data were expressed as (n, %). The χ^2 test was used for comparison. Differences were considered statistically significant at P < 0.05.

RESULTS

Comparison of the patients' surgical indicators between the two groups

Various intraoperative and postoperative indicators, such as operation time, intraoperative blood transfusion volume, and postoperative hospitalization duration time, were observed in the two groups for different surgical methods. It was found that the patients' intraoperative blood transfusion volume in the exploratory laparotomy + radical gastrectomy group was less than that in the palliative group. Furthermore, patients in the radical resection group had earlier off-bed activity and anus exhaust time. The differences had statistical significance (P < 0.05). However, there was no significant difference in operation time and postoperative hospitalization duration time between the two groups (P > 0.05). These findings unraveled that exploratory laparotomy + radical gastrectomy could reduce intraoperative blood transfusion volume and accelerate postoperative off-bed activity and anus exhaust, while radical gastrectomy did not affect the patient's recovery time (Table 2).

Comparison of the patients' incidence rate of postoperative complications between the two groups

Postoperative bleeding, duodenal stump rupture, anastomotic obstruction, intestinal obstruction, abdominal effusion, reflux gastritis, incision infection, and other complications were observed in the two groups that received different surgical treatments. The overall incidence rate of postoperative complications was not remarkably different between the two groups that received palliative therapy or laparotomy + radical gastrectomy, and the difference held no statistical significance (P > 1)

0.05). This suggested that the procedure of exploratory laparotomy + radical gastrectomy was safe and manageable (Table 3).

The patients' postoperative immune function in the two groups

The study discovered no substantial differences in the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ prior to operation between the radical resection and palliative groups (P > 0.05). Nevertheless, subsequent to the operation, CD3+, CD4+, CD3+/HLADR+, and CD4+/CD8+ levels were notably higher in the radical resection group than in the palliative group (P < 0.05). Furthermore, CD8+ levels in the palliative group after surgery were higher than before treatment (P < 0.05). Additionally, postoperative levels of IgG and IgM in the radical resection group were substantially increased to 18.35 \pm 2.16 and 3.87 \pm 0.53, respectively, which were significantly higher than the 14.68 \pm 2.28 and 3.56 \pm 3.19 Levels in the palliative group. The difference was regarded as statistically significant (P < 0.05). This finding suggested that the exploratory laparotomy + radical gastrectomy procedure could dramatically improve the patient's immune function (Table 4).

Comparison of the levels of postoperative tumor markers and inflammatory factors between the two groups

The outcomes revealed no noticeable difference in tumor markers CEA, CA199, and CA125 between the two groups prior to the operation (P > 0.05). However, at 12 wk after the operation, the levels of tumor markers were significantly lower in both groups, with a greater decrease observed in the radical gastrectomy group (P < 0.05). Specifically, the levels of CEA, CA199, and CA125 in the two groups were 7.72 ± 0.72 (ng/mL), 18.57 ± 3.15 (U/mL), and 34.34 ± 3.66 (U/mL), respectively. Similarly, there was no substantial difference in the levels of serum inflammatory factors IL-6, IL17, and TNF- α between the groups before surgery (P > 0.05). However, the levels of serum inflammatory factors IL-6, IL-17, and TNF- α were 27.47 ± 2.59 (pg/mL), 43.14 ± 5.69 (pg/mL), and 5.579 ± 0.46 (pg/mL), respectively, at 12 wk after the operation, which

were lower than those before treatment with a greater decrease observed in the radical gastrectomy group (P < 0.05). This finding confirmed that exploratory laparotomy + radical gastrectomy could considerably attenuate inflammatory reactions, while both surgical methods could vigorously enhance the levels of tumor markers, controlled tumor factors, and inflammatory factors. Moreover, the radical gastrectomy group exhibited more evident improvement than the palliative therapy group (Table 5).

Comparison of surgical efficacy and postoperative quality of life between the two groups

The research discovered an increase in ORR and DCR in the radical resection group group as opposed to the palliative group, and the difference had statistical significance (P < 0.05). Besides, the recovery of living quality was observed in the two groups undergoing various treatment methods. After the surgery, it was observed that the rate of improvement of patient's quality of life was 50% for the radical resection group, and the effective rate was 80.43%. In comparison, the rate of improvement of patient's quality of life in the palliative group was 23.26%, and the effective rate was 58.14%. The data for the radical resection group was higher than that of the palliative group, and the difference contained statistical significance (P < 0.05). This denoted that exploratory laparotomy + radical gastrectomy could enhance the rate of disease control and improve patients' quality of life after surgery (Table 6).

Comparison of the patient's postoperative survival rate and tumor recurrence rate between the two groups

The survival and tumor recurrence rates were evaluated at 6 mo, 1 year, and 2 years post-operation. The findings demonstrated that the survival rate at 6 mo, 1 year, and 2 years after laparotomy + radical gastrectomy was 100%, 97.83%, and 86.96%, respectively, and the differences had statistical significance (P < 0.05). After 6 mo of follow-up, it was discovered that there existed no substantial difference in tumor recurrence rates between the two groups that received different surgeries (P > 0.05).

Nevertheless, after 1 and 2 years of follow-up, the tumor recurrence rate of patients undergoing exploratory laparotomy + radical gastrectomy was lower than that of patients undergoing palliative therapy, and the difference was deemed to be statistically significant (P < 0.05). This finding indicated that exploratory laparotomy + radical gastrectomy could improve the postoperative survival rate of patients and decrease the tumor recurrence rate (Table 7).

DISCUSSION

Previous studies have shown that the peak incidence of GC is around the age of 60 years, and patients often have a variety of chronic systemic diseases, which can complicate clinical treatment^[20,24]. Surgery remains the mainstay of treatment and has been shown to improve patients' five-year post-treatment survival rate^[25-27]. However, given the differences in physical function among patients, choosing an appropriate surgical procedure is crucial to improve prognosis.

Prior studies suggest that patients with GC have relatively low malignant tumor cell degree, and radical gastrectomy should be selected as far as possible under the premise of adapting to surgery, which can effectively improve the survival rate and prolong the survival time of patients^[28,29]. However, radical gastrectomy involves extensive clearance and can cause significant trauma, making it unsuitable for elderly patients with poor physical condition. Palliative therapy, on the other hand, can alleviate clinical symptoms quickly and reduce surgical risk^[17,30,31]. Therefore, we compared different patient indicators following various surgical procedures to identify a suitable approach for patients and improve postoperative recovery and quality of life.

In this research, a total of 89 patients who underwent either exploratory laparotomy + radical gastrectomy or palliative therapy were included. The study revealed that patients who underwent exploratory laparotomy + radical gastrectomy required significantly less intraoperative blood transfusion. This is likely because palliative therapy involves dealing with a large number of small vessels at the tumor separation interface, while radical gastrectomy, which combines gastrectomy and D2

lymphadenectomy, can protect vascular branches and reduce intraoperative blood loss during lesion resection in patients with GC[32,33]. Additionally, there was no difference in hospitalization duration between the two surgical procedures, suggesting that exploratory laparotomy + radical gastrectomy did not cause greater harm to patients or hinder their recovery. Bleeding, perforation, and pyloric obstruction are common complications following GC surgery[34]. However, this study found no significant difference in the overall incidence of complications such as obstruction, reflux gastritis, and incision infection between patients who underwent exploratory laparotomy + radical gastrectomy and those who received palliative therapy. Moreover, the postoperative off-bed activity time and anus exhaust time were earlier than those of patients who underwent palliative therapy, which reduced the likelihood of postoperative incision infection and ensured that overall surgical safety remained within the controllable range.

Studies have shown that postoperative tissue injury can lead to the release of immunosuppressive agents, which may slow down the progression of tumor diseases^[35]. Here, we aimed to investigate the impact of two different surgical procedures on the immune function of patients with GC. We discovered that tissue injury caused by radical gastrectomy and palliative therapy had a certain impact on the immune function of patients. However, immune factors such as CD3+, CD4+, and CD8+ and immune proteins such as IgG and IgM were vigorously boosted subsequent to exploratory laparotomy + radical gastrectomy by contrast to patients undergoing palliative therapy, and these improved indicators reflected the recovery of T lymphocyte function and the enhancement of body resistance ability in patients were conducive to promoting the cellular immune function of patients. This may be related to early postoperative enteral nutrition support in patients undergoing radical gastrectomy for GC, which is superior to parenteral nutrition, regulates the metabolic and immune function of the body, corrects the immunosuppression triggered by surgical trauma, and improves the prognosis^[8,36].

CA199 is a macromolecular glycoprotein that contains mucinous components, and its level is correlated with tumor size, lymph node metastasis, and depth of invasion. It is an independent prognostic indicator for GC patients, with high levels in the serum indicating shortened survival time^[37]. Similarly, CEA is a polysaccharide-rich protein complex and a carcinoembryonic antigen produced during embryonic and fetal stages. It has prognostic significance for GC and is associated with progressive poorly differentiated adenocarcinoma, tumor size, serosal surface invasion, and lymph node metastasis[38]. Furthermore, CA125, a glycoprotein tumor-associated antigen, has great clinical value in the diagnosis of ovarian cancer and shows positive reactions in other malignant tumors, such as GC, cervical cancer, and breast cancer^[39]. We detected the levels of these tumor markers and found that the levels were higher in patients before radical gastrectomy and palliative therapy but significantly lower in both groups at 12 wk after surgery. CEA, CA199, CA125, and other markers significantly improved in patients who underwent exploratory laparotomy + radical gastrectomy compared to those in the palliative therapy group. Moreover, the levels of inflammatory factors were significantly lower than those in the palliative therapy group, suggesting that radical gastrectomy could ameliorate the tumor, control the enhancement of tumor factors, and heighten the level of inflammation. This finding has high clinical application value.

Adenocarcinoma is the primary pathological type in patients with GC, while poorly differentiated adenocarcinoma is infrequent. Hence, clinical exploratory laparotomy + radical gastrectomy can prolong the survival time of patients. Additionally, this study found that radical gastrectomy did not increase operative mortality despite being more traumatic^[40,41]. Du *et al*^[42] also found that radical gastrectomy was performed to thoroughly dissect lymph nodes and other debris to eliminate the risk of residual and recurrent lesions. The outcomes of this research showed that the survival rates of follow-up at 6 mo, 1 year, and 2 years in the radical resection group were significantly higher than those in the palliative group. The surgical efficacy was significantly better than that of the palliative group, and the postoperative quality of life was significantly improved compared with that of the palliative group, which indicated that exploratory

laparotomy + radical gastrectomy could effectively prolong the survival time of patients, improve the survival rate and significantly improve their quality of life compared with palliative therapy. It was consistent with the results of previous studies^[43,44]. More of note, the recurrence rate of tumors at 1 and 2 years of follow-up was significantly lower in patients who underwent exploratory laparotomy + radical gastrectomy than in the palliative group. This finding highlighted the potential benefits of exploratory laparotomy + radical gastrectomy, which can improve postoperative quality of life, reduce tumor recurrence, and improve patient prognosis.

To summarize, patients with GC should carefully choose their treatment options due to their unique circumstances. This study concludes that exploratory laparotomy + radical gastrectomy boasts significant therapeutic benefits. Compared with palliative therapy, it effectively improves surgical efficacy and immune function, reduces levels of tumor markers and inflammatory factors, prolongs survival, and improves the quality of life while reducing tumor recurrence rates with controllable safety. This treatment should be widely applied while ensuring strict adherence to indications. However, the retrospective nature of this study limited its scope and design. The 2-year survival rate observation was relatively short, and long-term survival status could not be assessed. Future studies should employ a more rigorous and systematic design to supplement and confirm these findings.

CONCLUSION

Laparotomy + radical gastrectomy is a preferable treatment over palliative therapy for GC patients suffering from upper digestive hemorrhage. It can enhance surgical efficacy, improve immune function, reduce tumor markers and inflammatory factors levels, prolong patient survival, improve quality of life, and lower the recurrence rate with controllable safety. The treatment is appropriate for patients with appropriate medical conditions.

ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) is a malignant tumor that originates from the gastric mucosal epithelium, and it has the highest incidence rate among various malignant tumors in China. Surgery is the main clinical treatment for GC.

Research motivation

The incidence rate of GC is extremely high, and surgical treatment is the primary approach to curing this disease.

Research objectives

This study aims to explore the clinical value of giving radical surgery and palliative surgery based on exploratory laparotomy in patients with GC combined with upper gastrointestinal bleeding.

Research methods

A total of 89 GC patients were selected and divided into two groups - the palliative group and the radical resection group. The two groups were compared in terms of various indicators such as the operation time, intraoperative blood transfusion, postoperative anal exhaust time, bed time, duodenal stump rupture, anastomotic obstruction complications, and the postoperative immune function, immunoglobulin and tumor markers, inflammatory factors, surgical effect, postoperative quality of life recovery, as well as patient monitoring for postoperative survival and tumor recurrence.

Research results

The radical resection group had shorter intraoperative blood loss and anal exhaust time compared to the palliative group, but did not show a significant difference in the occurrence of postoperative complications. Additionally, the postoperative immune function index and immunoglobulin levels of the radical resection group were higher

than those of the palliative group, while the levels of tumor markers and inflammatory factors were lower in the radical resection group. The surgical efficacy and postoperative quality of life of the radical resection group were also higher than those of the palliative group, and the postoperative survival rate was also higher for the radical resection group.

Research conclusions

Laparotomy combined with radical surgery can result in a shorter postoperative hospital stay, improved immune function, increased surgical efficacy, enhanced quality of life recovery, higher survival rate, and reduced chance of tumor recurrence.

Research perspectives

Due to the particularity of GC patients, they must be careful in selecting their treatment approach. Laparotomy combined with radical surgery can effectively enhance surgical efficacy, improve immune function, reduce tumor recurrence rate, and provide a safe and controllable treatment option. Therefore, this approach is worth promoting and applying. On the premise of strictly controlling the indications, laparotomy combined with radical surgery should be selected whenever possible.

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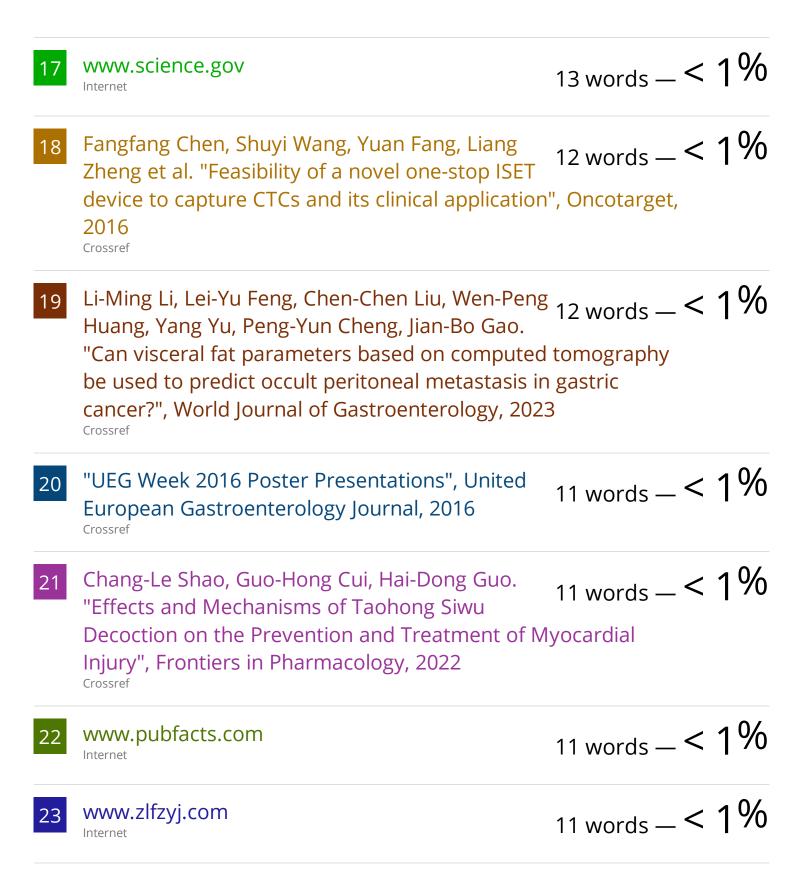
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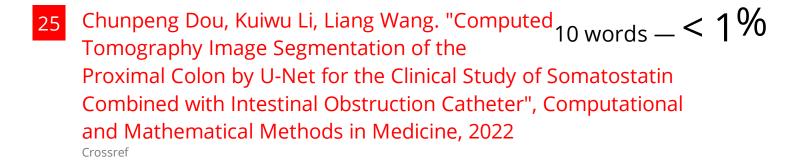
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