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# Pathological features and survival analysis of gastric cancer patients with positive surgical margins: A large multicenter cohort study

Ru-Hong Tu [a, b, 1], Jian-Xian Lin [a, b, 1], Wei Wang [e, 1], Ping Li [a, b, c, d], Jian-Wei Xie [a, b], Jia-Bin Wang [a, b], Jun Lu [a, b], Qi-Yue Chen [a, b], Long-long Cao [a, b], Mi Lin [a, b], Chao-Hui Zheng [a, b, c, d, **], Zhi-wei Zhou [e, ***], Chang-Ming Huang [a, b, c, d, *]

[a] Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou, China
[b] Department of General Surgery, Fujian Medical University Union Hospital, Fuzhou, China
[c] Key Laboratory of Ministry of Education of Gastrointestinal Cancer, Fujian Medical University, Fuzhou, China
[d] Fujian Key Laboratory of Tumor Microbiology, Fujian Medical University, Fuzhou, China
[e] Department of Gastric and Pancreatic Surgery, Sun Yat-sen University Caner Center, Guangzhou, China

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ABSTRACT

*Objective:* To investigate the factors related to positive surgical margins of gastric cancer and their correlation with the prognosis of these patients.
*Methods:* The clinicopathological data of gastric cancer patients undergoing gastrectomy were collected, and the relationship between surgical margins status and patient outcome was analyzed.
*Results:* A total of 10080 patients were included, among which 311 (3.1%) had positive surgical margins. pT3-4, pN+ and M1 were independent risk factors for positive margins, and a tumor in the middle of the stomach was a protective factor ($p < 0.05$). The 5-year overall survival (OS) rates of the patients with positive and negative margins after propensity score matching (PSM) were 24.2% and 36.8%, respectively ($p < 0.001$). For M0 patients, the 5-year OS of the margin-positive patients was lower than that of the margin-negative patients, and was higher than that of patients with M1. For the M1 patients, no statistically significant difference in 5-year OS was noted between patients with positive and negative margins. Age, positive margins, tumor location, pN+, and M1 were independent prognostic factors for OS in patients undergoing gastrectomy, and pN2-3 and M1 stages were independent prognostic factors for patients with positive surgical margins. Postoperative chemotherapy could improve the 5-year OS in pN2-3 and M1 margin-positive patients ($p < 0.05$).
*Conclusion:* The prognosis of M0 gastric cancer patients with positive surgical margins is poor, and it is recommended that these patients should undergo routine intraoperative frozen-section pathological examination to reduce the risk of positive surgical margins.


## Introduction

Gastric cancer remains an important disease to the threat of human health despite the fact that its incidence and mortality have declined [1–4]. The incidence of gastric cancer currently ranks as forth among other tumors, making it the second leading cause of death from cancer [5]. Surgical resection is currently the only treatment that may cure gastric cancer. Complete surgical resection, or R0 resection, is the goal of the surgery. However, adequate margins cannot be guaranteed due to tumor complications occurring during emergency surgery, such as hemorrhage, perforation, and obstruction, in patients with locally advanced or M1 gastric

* Corresponding author. Department of Gastric Surgery, Fujian Medical University Union Hospital, No.29 Xinquan Road, Fuzhou, 350001, China.
** Corresponding author. Fujian Key Laboratory of Tumor Microbiology, Fujian Medical University, Fuzhou, China.
*** Corresponding author.
*E-mail addresses:* wwkzch@163.com (C.-H. Zheng), zhouzhw@sysucc.org.cn (Z.-w. Zhou), hcmlr2002@163.com (C.-M. Huang).
[1] Tu RH, Lin JX and Wang W contributed equally to this work and should be considered co-first authors.

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cancer. In clinical work, the possibility exists that the final histopathological examination will show positive surgical margins even in patients with adequate surgical margins or in those with intraoperative negative frozen-sections margins. It has been reported that the incidence of positive margins after gastric cancer surgery ranges from 2.8% to 8.2% [6–10]. Some studies have demonstrated that the overall prognosis for patients with positive margins is poor [7–10]. However, most of these studies have been based on single-center case data, with the number of patients with positive margins being small; also, most of the cases used were at an advanced stage, and no comparison with patients in the same stage of disease was conducted. Therefore, the correlation between positive margins and the prognosis of patients at the same pathological stage has rarely been studied. The present study was designed to investigate the factors related to positive surgical margins and their correlation with long-term survival of gastric cancer patients in a large multicenter cohort study.

## Materials and methods

The clinicopathological data of gastric cancer patients admitted to the Department of Gastrointestinal Surgery, Fujian Medical University Union Hospital (FMUUH) between Jan. 1995 and Dec. 2016 and the Sun Yat-sen University Cancer Center (SYSUCC) between Jan. 2000 and Dec. 2014 who were diagnosed with primary gastric cancer and treated with gastric cancer resection were prospectively collected and retrospective analyzed. Tumor staging was performed according to the UICC staging standard for TNM staging (8th edition of 2016) [11].

Routine intraoperative frozen sections were performed in all patients of this study. In general, the resection of margin was based on the Japanese classification of gastric carcinoma: 3rd English edition [12]. The full circle, full-thickness sampling of proximal and distal margins would be sectioned serially at 2–5 mm that includes the closest resection margin of the specimen. “Positive margin” means that residual tumor in frozen section was founded. “Negative margin” was defined as no residual tumor in frozen section. And the Hematoxylin-eosin (H&E)-stained pathological sections of margin sampling was used [13].

The inclusion criteria were as follows: (1) Patients pathologically confirmed to have primary gastric adenocarcinoma prior to surgery. (2) Tumors planned for radical gastrectomy with no direct invasion of the surrounding organs, including the pancreas, spleen, and liver; no distant metastases to the liver, lung, or abdominal cavity; and no marked enlarged lymph nodes around the abdominal aorta, as demonstrated by preoperative chest radiography, abdominal ultrasound and abdominal CT examinations. (3) Preoperative tumors involving the esophagus or duodenum, requiring intraoperative exploration combined with frozen-section results to choose radical or palliative surgery. (4) Tumors with preoperative complications, such as tumor hemorrhage, obstruction, and perforation, for emergency operation. (5) Undergoing total, proximal or distal gastrectomy with lymph node dissection and digestive tract reconstruction. The exclusion criteria were as follows: (1) Intraoperative findings of peritoneal dissemination or distant metastasis, with no tumor hemorrhage, obstruction, perforation, or palliative resection. (2) Patients with neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy. (3) Patients with incomplete pathological diagnosis and follow-up data.

### *Follow-up*

All follow-up data were collected by two well-trained research assistants at the time of patient discharge and updated after each follow-up visit. The data were reviewed by a chief physician prior to analysis. The median follow-up time was 70 months in FMUUH and that for SYSUCC was 63 months, with an interval of 3–6 months. Overall survival (OS) time was calculated as the period from the diagnosis of gastric cancer to death from any cause.

### *Statistical analysis*

Continuous variables were analyzed using the Mann-Whitney *U* test, and categorical variables were analyzed using a $\chi 2$ test or Fisher's exact test. The survival rate was calculated, and a survival curve was plotted using the Kaplan-Meier method. The survival rates were compared by log-rank tests. A 1:3 propensity score matching (PSM) was applied in the present study to reduce bias [14]. Specifically, center, age, sex, tumor size, tumor location, T stage, N stage, and the presence of distant metastasis were taken as variables, and a logistic regression model was used to calculate the propensity score for each patient. Patients undergoing laparoscopic or open surgeries with similar scores were matched at a ratio of 1:3 in accordance with the “principle of proximity”. A p-value of $<0.05$ was considered statistically significant. The SPSS 18.0 statistical software package (version 18.0, SPSS Inc, Chicago, IL) was used for data analysis.

## Results

### *Occurrence of positive margins*

Data from a cohort of patients in two centers were included in this study, and a total of 10080 patients who underwent radical gastrectomy were enrolled, including 6406 from FMUUH and 3674 from SYSUCC. Positive surgical margins were observed in 311 (3.1%) as shown in Supplement Fig. 1. The general clinicopathological data of patients with negative (Mar0) and positive margins (Mar1) are summarized in Supplement Table 1. Compared with Mar0 patients, Mar1 patients had a larger tumor diameter, a higher proportion of proximal tumors and tumors located in $\geq$2 sites in the stomach, more advanced pTNM stage, and a higher proportion of undifferentiated cancers.

Differences in general clinical and pathological factors between two groups of patients may lead to bias. Therefore, PSM was applied in the present study, and 311 patients with positive margins and 933 with negative margins were identified, which is a ratio of 1:3. No statistically significant differences in the clinical and pathological factors were found between these two groups.

### *Risk factors associated with positive margins*

Univariate analysis of the potential related factors for positive surgical margins in the whole group showed that tumor size, tumor location, T stage, N stage and M stage were correlated with the occurrence of positive margins. Multivariate analysis of the factors with $p < 0.010$ in the univariate analysis demonstrated that T3-4, N+ and M1 were independent risk factors for positive margins and a tumor in the middle of the stomach was a protective factor ($p < 0.05$), as shown in Table 1.

### *Survival of patients with gastric cancer*

The five-year OS rate of the patients with positive margins was 24.2% before PSM, which was significantly different from that of the patients with negative margins (57.9%, $p < 0.001$, Fig. 1A). After PSM, the 5-year OS of the patients with positive and negative margins were 24.2% and 36.8%, respectively ($p < 0.001$, Fig. 1B).

**Table 1**
Univariate and multivariate analysis of risk factors for positive margins.

| Variables | Univariate analysis | | | | Multivariate analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | HR | 95%CI | | p value | HR | 95%CI | | p value |
| Age | 0.994 | 0.982 | 1.006 | 0.336 | / | | | |
| Gender(M vs. F) | 0.981 | 0.709 | 1.357 | 0.907 | / | | | |
| Tumor diameter | | | | | | | | |
| <20 mm | Ref | | | | Ref | | | |
| ≥20 mm,<50 mm | 5.103 | 2.044 | 12.740 | 0.000 | 1.417 | 0.550 | 3.647 | 0.470 |
| ≥50 mm | 13.368 | 5.461 | 32.725 | 0.000 | 2.317 | 0.910 | 5.900 | 0.078 |
| Tumor location | | | | | | | | |
| Upper1/3 | Ref | | | | Ref | | | |
| Middle1/3 | 0.398 | 0.238 | 0.665 | 0.000 | 0.399 | 0.238 | 0.670 | 0.001 |
| Lower1/3 | 0.608 | 0.428 | 0.864 | 0.006 | 0.799 | 0.559 | 1.143 | 0.219 |
| ≥2 areas | 1.750 | 1.211 | 2.528 | 0.003 | 1.286 | 0.880 | 1.879 | 0.194 |
| p T | | | | | | | | |
| T1-2 | Ref | | | | Ref | | | |
| T3-4 | 30.610 | 9.776 | 95.843 | 0.000 | 11.078 | 3.354 | 36.583 | 0.000 |
| p N | | | | | | | | |
| N0 | Ref | | | | Ref | | | |
| N+ | 8.666 | 4.708 | 15.950 | 0.000 | 3.078 | 1.637 | 5.786 | 0.000 |
| M1 | 3.944 | 2.397 | 6.489 | 0.000 | 2.234 | 1.342 | 3.720 | 0.002 |

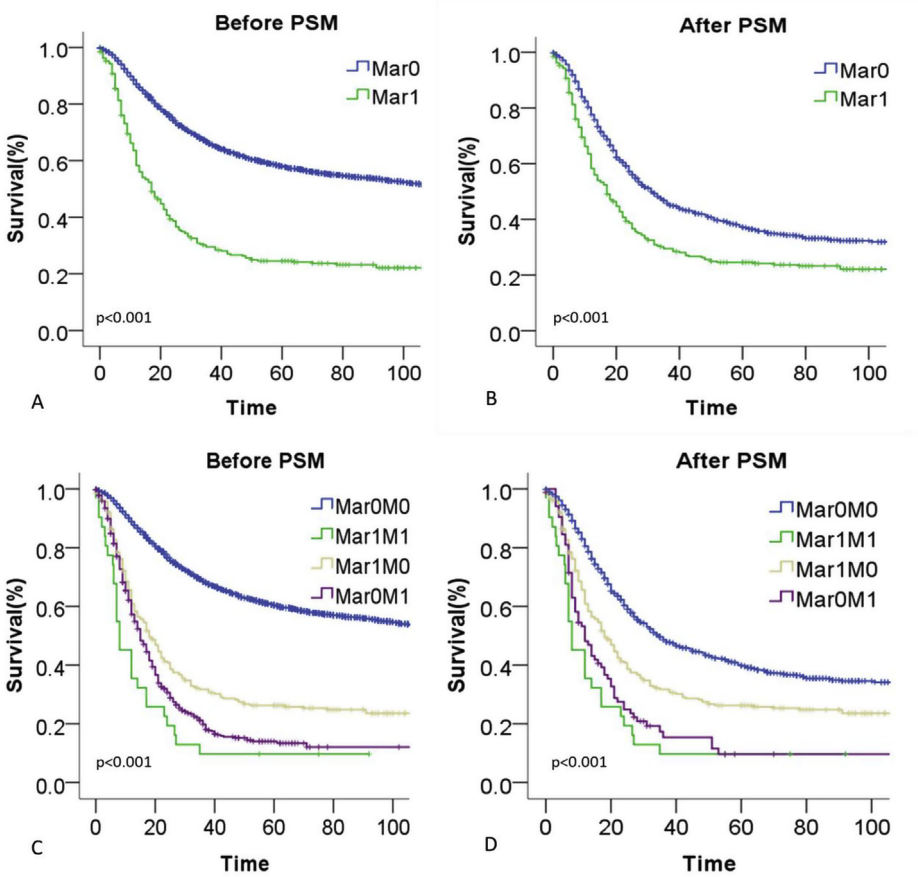


**Fig. 1.** Kaplan-Meier Overall survival (OS) among patients with negative (Mar0) and positive (Mar1) margin: A. Before PSM, $p < 0.001$; B. After PSM, $p < 0.001$; among patients with negative margin without metastasis (Mar0M0), positive margin without metastasis (Mar1M0), negative margin with metastasis (Mar0M1), and positive margin with metastasis (Mar1M1): C. Before PSM, $p < 0.001$; D. After PSM, $p < 0.001$.

*Effect of positive margins on the prognosis of M0 or M1 patients*

All patients were divided into 4 subgroups, i.e., the negative margin without metastasis (Mar0M0) group, the positive margin without metastasis (Mar1M0) group, the negative margin with metastasis (Mar0M1) group, and the positive margin with metastasis (Mar1M1) group, and their 5-year OS rates were 60.3%, 25.8%, 13.4%, and 9.7%, respectively, before PSM ($p < 0.001$), and 40.2%, 25.4%, 9.0%, and 9.7%, respectively, after PSM ($p < 0.001$, Fig. 1). The 5-year OS of Mar1M0 patients was lower than that of Mar0M0 and higher than that of Mar0/1M1 patients before and after PSM ($p < 0.05$, Fig. 1).

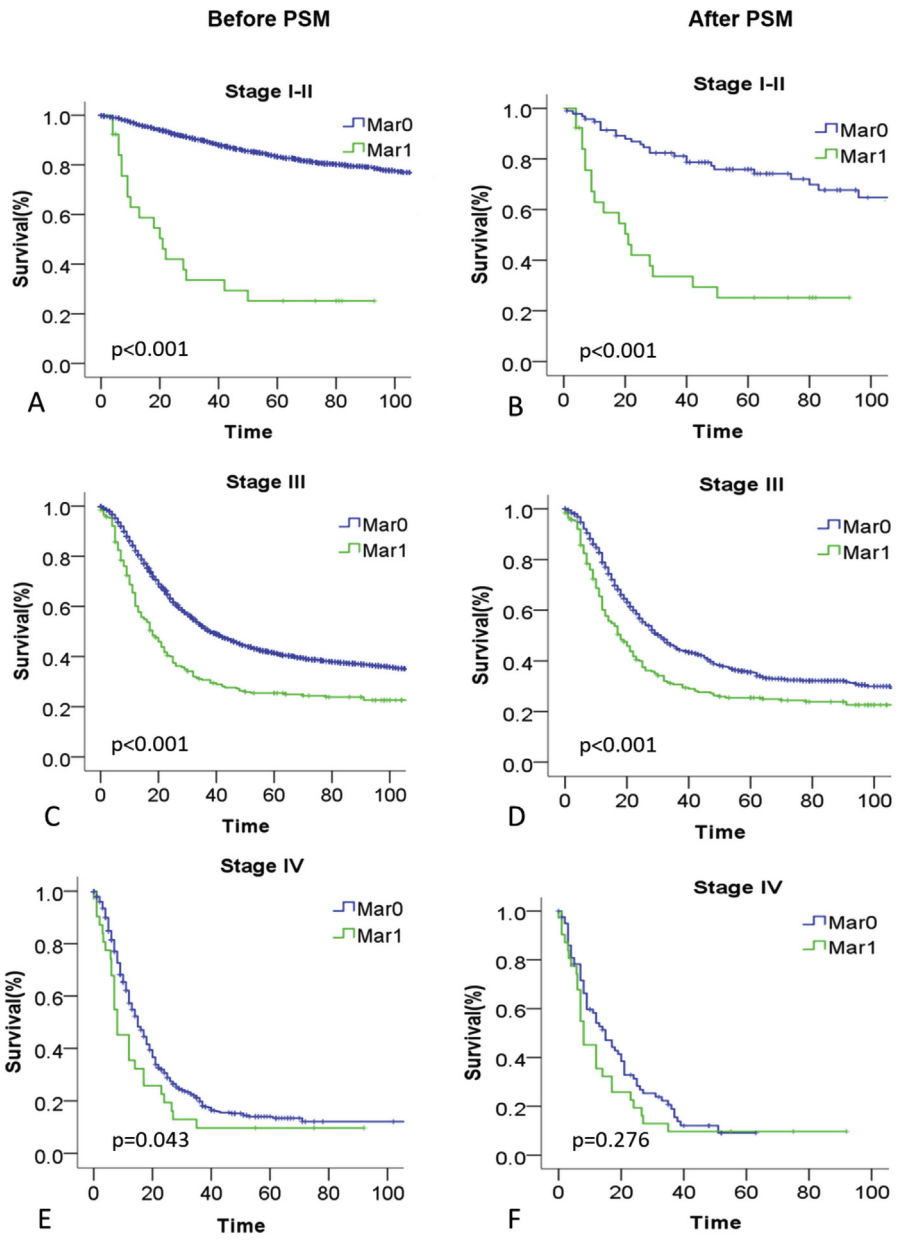


**Fig. 2.** Kaplan-Meier Overall survival (OS) among three stages. A. Stage I-II, $p < 0.001$; B. Stage I-II, $p < 0.001$; C. Stage III, $p < 0.001$; D. Stage III, $p < 0.001$; E. Stage IV, $p = 0.043$. F. Stage IV, $p = 0.276$.Panels A,C,E shows before PSM, Panels B,D,F shows after PSM.

Stratified analysis of the difference in survival rates between patients with negative and positive margins was carried out based on pTNM stages, as shown in Fig. 2. Patients with stage I and II were pooled and analyzed due to the small number of such patients. The 5-year OS of I–IV stage Mar1 patients before PSM was lower than that of Mar0 patients at the same stage ($p < 0.05$), and the difference was statistically significant. After PSM, the 5-year OS of Mar1 Stage I–III patients was lower than that of Mar0 stage I–III patients ($p < 0.05$), and the difference in the 5-year OS between stage IV Mar1 and Mar0 patients was not statistically significant ($p = 0.276$, Fig. 2).

*Analysis of prognostic factors after PSM*

Factors that affected the OS of patients with gastric cancer resection after PSM were analyzed and are summarized in Table 2. The results showed that age, margin status, tumor location, N stage, and M stage were independent risk factors for OS in patients with gastric cancer resection ($p < 0.05$). The analysis of the prognostic factors of OS in patients with positive margins is shown in Table 3, and the results indicate that pN2-3 and M1 are independent prognostic factors for OS in margin-positive patients ($p < 0.05$).

*Effect of chemotherapy on margin-positive patients*

Data from the patients who received at least one cycle of 5-Fu-based chemotherapy were also recorded in the FMUUH database. Among all of the FMUUH patients, 201 patients were margin-positive, among which 122 received postoperative chemotherapy and 79 did not. No significant differences in sex, age, tumor size, or TNM staging were found between the two groups of patients ($p < 0.05$, Supplement Table 2). There was no significant difference

**Table 2**
Univariate and Multivariate Analyses for Overall Survival in patients after gastrectomy of gastric cancer (After PSM).

| Variables | Univariate analysis | | | | Mutivariates analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | HR | 95%CI | | p value | HR | 95%CI | | p value |
| Age | 1.009 | 1.003 | 1.015 | 0.002 | 1.013 | 1.007 | 1.019 | 0.000 |
| Gender(M vs. F) | 0.988 | 0.856 | 1.141 | 0.872 | / | | | |
| Mar1 vs. Mar0 | 1.594 | 1.368 | 1.857 | 0.000 | 1.529 | 1.31 | 1.783 | 0.000 |
| Tumor diameter | 1.004 | 1.002 | 1.006 | 0.000 | 1.006 | 0.999 | 1.014 | 0.098 |
| Tumor location | | | | | | | | |
| Upper1/3 | Ref | | | | Ref | | | |
| Middle1/3 | 1.042 | 0.847 | 1.282 | 0.697 | 0.86 | 0.694 | 1.067 | 0.171 |
| Lower1/3 | 0.845 | 0.706 | 1.012 | 0.067 | 0.818 | 0.682 | 0.982 | 0.031 |
| ≥2 areas | 1.330 | 1.098 | 1.612 | 0.004 | 1.084 | 0.883 | 1.33 | 0.442 |
| p T | | | | | | | | |
| / | | | | | | | | |
| T1 | Ref | | | | / | | | |
| T2 | 1.452 | 0.414 | 5.094 | 0.561 | / | | | |
| T3 | 2.350 | 0.739 | 7.479 | 0.148 | / | | | |
| T4a | 2.937 | 0.944 | 9.139 | 0.063 | / | | | |
| T4b | 2.951 | 0.945 | 9.217 | 0.063 | / | | | |
| p N | | | | | | | | |
| N0 | Ref | | | | Ref | | | |
| N1 | 2.302 | 1.546 | 3.427 | 0.000 | 2.108 | 1.414 | 3.142 | 0.000 |
| N2 | 2.476 | 1.724 | 3.556 | 0.000 | 2.254 | 1.568 | 3.24 | 0.000 |
| N3a | 2.859 | 2.020 | 4.047 | 0.000 | 2.692 | 1.901 | 3.812 | 0.000 |
| N3b | 4.065 | 2.883 | 5.732 | 0.000 | 3.845 | 2.726 | 5.423 | 0.000 |
| Undifferentiated type | 0.986 | 0.848 | 1.147 | 0.858 | / | | | |
| LBVI | 1.235 | 1.002 | 1.521 | 0.047 | 0.915 | 0.732 | 1.144 | 0.436 |
| M1 | 2.340 | 1.880 | 2.913 | 0.000 | 2.267 | 1.817 | 2.828 | 0.000 |

**Table 3**
Univariate and Multivariate Analyses for Overall Survival in margin-positive patients.

| Variables | Univariate analysis | | | | Mutivariates analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | HR | 95%CI | | p value | HR | 95%CI | | p value |
| Age | 1.007 | 0.996 | 1.018 | 0.194 | / | | | |
| Gender(M vs. F) | 1.103 | 0.849 | 1.434 | 0.462 | / | | | |
| Tumor diameter | 1.001 | 0.997 | 1.005 | 0.566 | / | | | |
| Tumor location | | | | | / | | | |
| Upper1/3 | Ref | | | | Ref | | | |
| Middle1/3 | 1.014 | 0.656 | 1.567 | 0.950 | 0.848 | 0.538 | 1.336 | 0.477 |
| Lower1/3 | 1.062 | 0.767 | 1.469 | 0.718 | 0.974 | 0.701 | 1.355 | 0.877 |
| ≥2 areas | 1.514 | 1.085 | 2.112 | 0.015 | 1.204 | 0.835 | 1.734 | 0.320 |
| p T | | | | | | | | |
| T1-2 | Ref | | | | Ref | | | |
| T3 | 0.524 | 0.219 | 1.257 | 0.148 | 0.341 | 0.138 | 0.844 | 0.020 |
| T4a | 0.511 | 0.239 | 1.093 | 0.084 | 0.313 | 0.141 | 0.694 | 0.004 |
| T4b | 0.435 | 0.199 | 0.951 | 0.037 | 0.284 | 0.126 | 0.640 | 0.002 |
| p N | | | | | | | | |
| N0 | Ref | | | | Ref | | | |
| N1 | 1.682 | 0.854 | 3.312 | 0.133 | 1.891 | 0.947 | 3.776 | 0.071 |
| N2 | 1.772 | 0.977 | 3.215 | 0.060 | 1.861 | 1.016 | 3.408 | 0.044 |
| N3a | 1.750 | 0.983 | 3.118 | 0.057 | 1.926 | 1.061 | 3.498 | 0.031 |
| N3b | 2.692 | 1.528 | 4.743 | 0.001 | 3.010 | 1.672 | 5.420 | 0.000 |
| Undifferentiated type | 0.868 | 0.651 | 1.159 | 0.338 | / | | | |
| LBVI | 1.254 | 0.853 | 1.844 | 0.249 | / | | | |
| M1 | 1.849 | 1.244 | 2.748 | 0.002 | 1.830 | 1.228 | 2.728 | 0.003 |

in 5-year OS between margin-positive patients with and without postoperative chemotherapy ($p = 0.158$, Fig. 3). In the stratified analysis, however, the forest plot of the risk of chemotherapy-related death (OR) for margin-positive patients showed that the 5-year OS of pN2-3 (OR = 0.685, $p = 0.028$) and M1 (OR = 0.216, $p = 0.007$) patients was improved after postoperative chemotherapy (Supplement Fig. 2).

*Survival for positive proximal and distal margins*

The difference in outcomes between patients with positive proximal and distal margins was further analyzed in this study, and the results showed that of the 201 FMUUH patients with positive margins, there were 112 cases with positive proximal margins (Pro), 71 with positive distal margins (Dis), and 18 with both positive proximal and distal margins (Bot). No statistically significant difference in the 5-year OS was observed among the three groups ($p = 0.161$) or between the Pro and Dis groups ($p = 0.071$) (Supplementary Fig. 3).

## Discussion

Currently, no consensus on the length of the resection margin that is adequate for the radical resection of gastric cancer has been

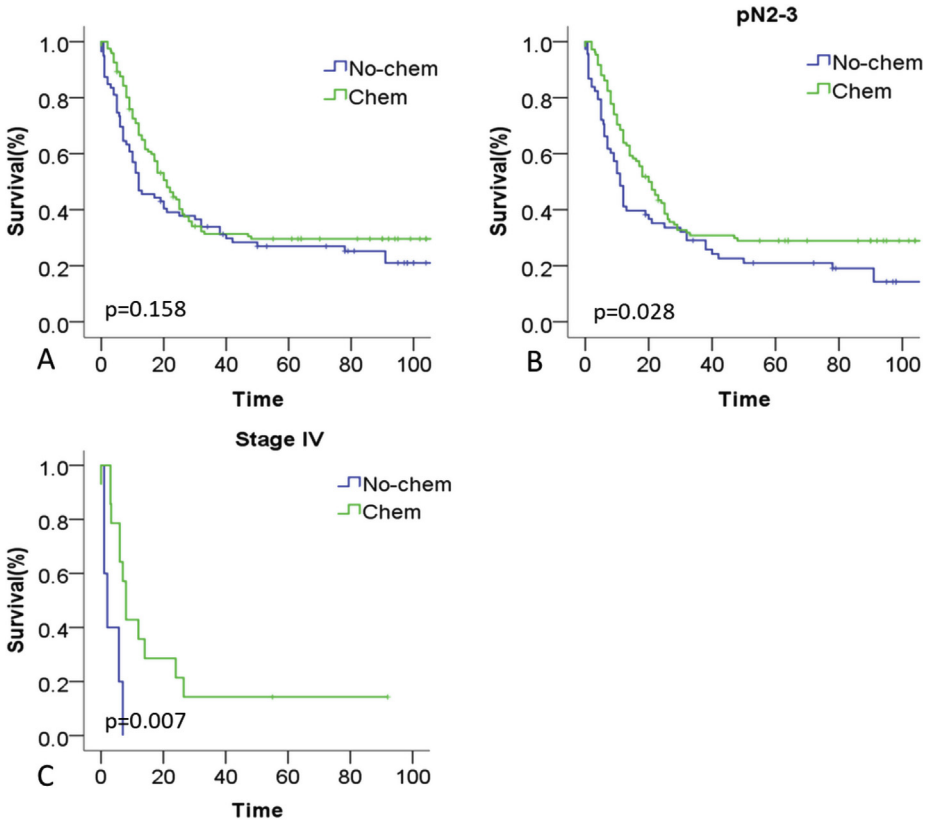


**Fig. 3.** Kaplan-Meier Overall survival (OS) among margin-positive patients with or without chemotherapy in FMUUH: A. All patients, p = 0.158; B. pN2-3, p = 0.028; C. Stage IV, p = 0.007.

reached. The NCCN Guidelines recommend that a margin of ≥4 cm is required for patients with T1-T3 disease, and the whole lesion involved needs to be resected for stage T4 patients [15]. Japanese gastric cancer treatment guidelines require that the length of resection margins for stage T1, stage T2 and above with Borrman type I and II, and stage T2 and above with Borrman type III and IV patients should be > 2 cm, >3 cm, and >5 cm, respectively; for patients whose margins cannot be defined, the extent of resection should be determined based on the intraoperative frozen-section results [16]. These variations have brought about a certain confusion among clinicians in practice. Adequate margins cannot be guaranteed sometimes due to tumor complications, such as hemorrhage, perforation, and obstruction, in patients with locally advanced or M1 gastric cancer, and it is also possible that the final histopathological examination will show positive surgical margins in patients with adequate surgical margins, even in those with negative intraoperative frozen-section margins. Therefore, a positive surgical margin is an issue that every surgeon must face and it is sometimes difficult to avoid. It has been reported previously that the incidence of positive margins after gastric cancer surgery ranges from 2.8% to 8.2% [6–10], and it was 3.1% in the present study.

Factors associated with positive surgical margins in patients with gastric cancer still remain unclear. Wang et al. [10] believed that inadequate margins caused by surgical techniques may not be the real explanation for positive margins; some researchers, however, have demonstrated that a higher proportion of positive margins is often found in patients with factors including larger tumor diameter, deeper infiltration (T) and advanced TNM Stage [10,17,18]. Shen et al. [19] showed that compared with postoperative pathology, the accuracy, sensitivity, and specificity of intraoperative frozen-section examination in patients with proximal gastric cancer were increased to 97%, 77.8%, and 100%, respectively, making it the most effective method currently available for determining the margin status. Scholars recommend that frozen-section examination should be routinely performed for patients during gastric cancer resection, especially for those with T3-4 tumors [10,16,19]. It was verified in our present study that stage T3-4 tumors were prone to positive surgical margins and we found that lymph node metastasis and M1 were also independent risk factors for positive margins, while carcinoma of the middle stomach was a protective factor. Therefore, it is recommended for gastric cancer patients with no distant metastasis and no middle stomach disease to routinely undergo intraoperative frozen-section examination when there are findings of T3-4 and lymph node enlargement in order to reduce the risk of positive surgical margins. However, the prognosis differs greatly depending on the presence of margin involvement in stage I-II as shown in Fig. 2. The superficially spreading (Super) type of growth pattern could be found in early gastric cancer, designated as one with a diameter >4.0 cm, was either confined to the mucosa or had partly invaded the submucosa [20,21]. So the adequate margin is hard to decide also in early gastric cancer patients that the frozen examination is necessary. Additionally, the data of Lauren type was unavailable in this study. But according to previous studies, diffuse types were with a higher risk of poorly differentiated or undifferentiated cell type, a lower possibility of R0 surgical resection, and worse prognosis compared to intestinal types [22]. Therefore, the adequate margins and the frozen examination were needed for those patients.

Previous studies have shown that in addition to T-stage and N-stage, a positive surgical margin is an independent risk factor for a poor outcome among patients undergoing gastric cancer resection

[23–29]. However, a study by Cho et al. [28] found that a positive surgical margin is an independent prognostic factor for patients without lymph node metastasis, but not for those with lymph node metastasis. The results of the present study showed that a positive surgical margin is an independent prognostic factor for OS in patients undergoing gastric resection. Further stratified analysis based on TNM staging showed that positive surgical margins was correlated with the long-term outcome of patients with stage I–III gastric cancer. Moreover, it was also found in the present study that the outcome of margin-positive patients without distant metastases was better than that of patients with distant metastases. Therefore, patients with positive margins could not be easily treated as M1 patients when selecting a subsequent treatment. Among studies on prognostic factors in patients with positive surgical margins, those conducted by Cho [28] and Wang [10] concluded that the outcome of margin-positive patients with lymph node metastasis is worse. The results of the present study also suggest that pN2-3 and M1 are independent prognostic factors for OS in patients with positive margins.

The treatment of patients with positive surgical margins is one of the current key research topics, and no standard procedure is available to date. Some scholars believe that margin-positive patients with lymph node metastasis may clinically benefit from re-resection to achieve negative margins [11]. Wang et al. [10] however, showed that the recurrence of margin-positive patients are commonly in the form of distant metastases rather than local recurrence. Therefore, resection may not be beneficial to these patients.

When making a decision about subsequent therapies for patients with positive surgical margins, including radiotherapy, chemotherapy, and radiochemotherapy, clinicians usually refer to the adjuvant treatment plan for radical gastrectomy and their prescribing habits, due to the non-availability of direct studies on this issue. Our study showed that the 5-year OS of pN2-3 and M1 margin-positive patients was increased when chemotherapy was given, although chemotherapy may not improve the survival of all margin-positive patients. There is no evidence as to whether chemoradiotherapy can improve the prognosis of patients with positive margins or is better than radiotherapy or chemotherapy alone. Subsequent treatment approaches for patients with positive surgical margins needs more high-level evidence-based support.

There were limitations to this study. First, this was a retrospective study, and there were unavoidable unknown biases, although PSM was used to balance the differences between groups. The reliability of the results needs to be validated in large, multicenter, prospective clinical trials. Next, no specific values for the length of the surgical margins were provided in this study to analyze the ideal length of the margins. In addition, data on the recurrence site, time, and corresponding treatment of patients with positive margins were incomplete, and therefore their subsequent treatment could not be further studied. However, the present study may provide a preliminary basis for additional studies, such as those involving subsequent adjuvant therapy, in patients with positive margins.

In conclusion, the long-term prognosis of M0 gastric cancer patients with positive surgical margins is poor, and it is recommended that these patients should undergo routine intraoperative frozen-section pathological examination to reduce the risk of positive surgical margins.

## Authors' contributions

Ru-Hong Tu, Jian-Xian Lin, Wei Wang, Chao-Hui Zheng, Zhi-wei Zhou, Chang-Ming Huang, conceived the study, analyzed the data, and drafted the manuscript, Zhi-wei Zhou, Chao-Hui Zheng, Chang-Ming Huang helped critically revise the manuscript for important intellectual content. Jian-Xian Lin, Ping Li, Chao-Hui Zheng, Jian-Wei Xie, Jia-Bin Wang, Jun Lu, Qi-Yue Chen, Long-long Cao and Mi Lin helped collect data and design the study. All authors read and approved the final manuscript.

## Disclosures

There are no conflicts of interest or financial ties to disclose from any authors. The study was sponsored by the Scientific and technological innovation joint capital projects of Fujian Province (2016Y9031); Construction Project of Fujian Province Minimally Invasive Medical Center (No. [2017]171); The second batch of special support funds for Fujian Province innovation and entrepreneurship talents (2016B013).

## Conflict of interest statement

There are no conflicts of interest or financial ties to disclose from any authors.

## Ethical standards

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (The ethics committee of Fujian Union Hospital (Approval number: 20070428)) and with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.06.026.

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