Comparison of five tumor regression grading systems for gastric adenocarcinoma after neoadjuvant chemotherapy: a retrospective study of 192 cases from National Cancer Center in China

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Abstract

Background: Neoadjuvant chemotherapy has been increasingly practiced on gastric cancer (GC), and histological evaluation to predict outcome is urgent in clinical practice. There are five classic tumor regression grading (TRG) systems, including Mandard-TRG system, the Japanese Gastric Cancer Association (JGCA)-TRG system, College of American Pathologists (CAP)-TRG system, China-TRG system and Becker-TRG system.

Methods: Totally, 192 patients of gastric adenocarcinoma (including adenocarcinoma of the esophagogastric junction) treated by neoadjuvant chemotherapy and surgery were evaluated using the above five TRG systems. The clinicopathological characteristics were also assessed. The correlation among TRG systems, clinicopathological characteristics and prognosis were analyzed.

Results: All the five TRG systems were significantly correlated with differentiation, postsurgical T category, postsurgical N category, American Joint Committee on Cancer (AJCC) stage, lymph-vascular invasion, perineural invasion, as well as tumor size. All the five TRG systems were statistically significant in univariate Cox survival analysis. However, only postsurgical T category, postsurgical N category and R0 resection were independent in multivariate Cox survival analysis. The tight correlation between the TRG systems and other characteristics such as postsurgical stage might affect the independent prognostic role of the TRG systems. As compared with other TRG systems, the hazard ratio of no/slightly response in both Mandard TRG system and JGCA TRG system revealed higher hazard of death and disease progression than that of severe response when using univariate Cox survival analysis. The median survival time of complete response and nearly complete response were much longer than that of partial response, all classified by Mandard-TRG system. This could help clinicians predict prognosis more reasonably than JGCA-TRG which does not have the category of nearly complete response.

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**Background**

In 2012, 951,000 new diagnoses of gastric cancer (GC) and 723,000 GC deaths were calculated worldwide, accounting for 6.8% of all cancer incidence and 8.8% of all cancer mortality, respectively [1]. At present, GC is the second common cancer in China, while approximately 679,100 new cancer cases and 498,000 related deaths were estimated in China in 2015 [2]. The most promising curative treatment for GC is surgical resection. However, this treatment alone is not enough for curing advanced GC because of poor long-term outcome, thus a multimodality therapy is required. Nowadays, neoadjuvant chemotherapy has been increasingly used to prolong patient survival worldwide [3], therefore an effective histopathological evaluation method predicting patient prognosis is urgently needed in clinical practice. So far, four tumor regression grading (TRG) systems were presented by several studies. Mandard et al. proposed a five-tiered TRG system in esophageal carcinoma which has been used widely in digestive malignancy [4]. The Japanese Gastric Cancer Association (JGCA) suggested a different five-tiered grading system specifically for GC [5]. College of American Pathologists (CAP) recommended a simplified four-tiered grading system based on Mandard-TRG system [6]. In China, a three-tiered grading system has been used for solid malignancies to evaluate the extent of therapy-related tumor regression [7]. In recent years, Becker et al. recommended a four-tiered grading system for GC based on large number of patients and long-term follow-up [8, 9]. For the purpose of further evaluation of the relationship between TRG and prognosis, we retrospectively collected 192 patients in our hospital. We used the above five TRG systems to assess the pathological response respectively, trying to select a better histopathological evaluation system.

**Methods**

**Patients**

Between January 2007 and August 2013, 192 patients with locally advanced gastric adenocarcinoma (including adenocarcinoma of the esophagogastric junction) underwent gastrectomy in National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. All the patients received neoadjuvant chemotherapy previously. The treatment strategies were not uniform, and the drugs most used included oxaliplatin, cisplatin, docetaxel, 5-fluorouracil, and Tegafur Gimeracil Oteracil Potassium Capsule. There were 133 patients who received additional adjuvant chemotherapy after surgery. All cases had only one primary gastric tumor, except one patient, who had two primary lesions located at the fundus and antrum, separately. The tumor located at the fundus was evaluated in our study for its relatively higher T category. There were 139 male and 53 female, and the age ranged 31–77 years old (median age, 55 years old).

**Follow-up**

The mortality data was mainly gathered from clinical archives, or via telephone and mail. After treatment, patients were evaluated every 3 months for the first 2 years, and subsequently every 6 months for the following 3 years, and then annually according to institutional policy. Information of recurrence was updated every time the patients came for follow-up visits. The time of overall-survival (OS) was calculated from the first day of the neoadjuvant chemotherapy to the day when death occurred or to the last follow-up (September 2015). The time of progression-free-survival (PFS) was calculated from the first day of the neoadjuvant chemotherapy to the day when progression happened, death occurred or to the last follow-up (September 2015). Eleven patients were lost to follow-up. The median follow-up time was 31 months (4.1–95.3 months). Three patients, who died as the result of surgery complications, and 8 patients, whose follow-up time after surgery were less than 3 months, were excluded from the survival analysis.

**Assessment of the specimens**

If obvious residual carcinoma was identified macroscopically, the tumor specimen was sampled for at least 1 block per centimeter. If the maximum of residue was less than 3 cm or only areas of scar existed, the whole suspected lesion was submitted completely for histological examination. Four-micrometer sections were stained with hematoxylin and eosin. The average of slides per residual tumor was 9.7 (3–77), while the median number of the examined lymph nodes per case was 24 (3–58).
Clinicopathological characteristics
The clinicopathological features include tumor location, tumor size, histological differentiation, Laurén classification, lymph-vascular invasion (LVI) and perineural invasion (PNI). The tumor staging was based on the American Joint Committee on Cancer (AJCC) cancer staging 7th edition [10]. All the slides were reviewed by three experienced pathologists (YZ, JY and LX). In case of a disagreement about diagnosis, three pathologists reviewed the slides on a multi-headed microscope and reached a consensus diagnosis.

Tumor regression grading systems
The criteria of the five TRG systems are shown in Table 1.

Statistical analysis
Correlations between tumor regression evaluation systems and clinicopathological characteristics were performed by $\chi^2$ tests. And 2-sided $p$-values < 0.05 were considered statistically significant. The survival curve and median survival time were calculated using Kaplan-Meier method and log rank test. The univariate analysis of survival was evaluated by univariate Cox regression analysis. The statistic significant factors in univariate analysis were assessed by backward step-wise multivariate Cox regression analysis. Variables with a $p$-value of <0.05 were retained, and variables with a $p$-value of >0.10 were removed. All statistics were performed by SPSS 16.0 software (SPSS Inc, Chicago, IL).

Results
Clinicopathological characteristics
All the 192 patients received radical surgery. Forty-nine patients underwent proximal subtotal gastrectomy. Eighty-eight patients underwent distal subtotal gastrectomy. Fifty-three patients underwent total gastrectomy. Two patients underwent residual gastrectomy, both of which underwent distal gastrectomy previously due to severe ulcer. Sixty-three patients underwent D1 lymphadenectomy and 129 underwent D2 lymphadenectomy. The examined numbers of the removed lymph nodes per case ranged from 3 to 58. One-hundred and fifty-nine patients got R0 resection (82.8%). Twenty-one patients had local unresectable residues detected macroscopically by the surgeons while 12 had microscopic positive margins. Forty-four patients had

| TRG system | Grade | Description |
|------------|-------|-------------|
| Mandard-TRG | 1     | No residual cancer |
|            | 2     | Rare residual cancer cells |
|            | 3     | Fibrosis outgrowing residual cancer |
|            | 4     | Residual cancer outgrowing fibrosis |
|            | 5     | Absence of regressive changes |
| JGCA-TRG   | 0     | No evidence of effect |
|            | 1a    | Viable tumor cells occupy more than 2/3 of the tumorous area |
|            | 1b    | Viable tumor cells remain in more than 1/3 but less than 2/3 of the tumorous area |
|            | 2     | Viable tumor cells remain in less than 1/3 of the tumorous area |
|            | 3     | No viable tumor cells remain |
| CAP-TRG    | 0     | No viable cancer cells (complete response) |
|            | 1     | Single cells or small groups of cancer cells (moderate response) |
|            | 2     | Residual cancer outgrown by fibrosis (minimal response) |
|            | 3     | Minimal or no tumor killed or extensive residual cancer (poor response) |
| China-TRG  | Severe response | Tumor cells completely disappear or very few highly regressive residue exist with obvious scarring and varying inflammation |
|            | Moderate response | Most tumor cells degenerate and necrosis with obvious stroma fibrosis and inflammation |
|            | Mild response | Absence of or slight necrosis and degeneration of tumor cells accompanied by mild stroma fibrosis and inflammation |
| Becker-TRG | 1a    | No residual tumor/tumor bed |
|            | 1b    | <10% residual tumor/tumor bed |
|            | 2     | 10–50% residual tumor/tumor bed |
|            | 3     | >50% residual tumor/tumor bed |
| Characteristics                  | Total cases (n = 192), no. (%) | Mandard-TRG | P value |
|----------------------------------|---------------------------------|-------------|---------|
|                                 | 1 (n = 11), no. (%)             | 2 (n = 23), no. (%) | 3 (n = 40), no. (%) | 4 (n = 78), no. (%) | 5 (n = 40), no. (%) |
| Gender                          |                                |             |         |         |         |
| Male                            | 139 (72.4)                     | 10 (7.2)    | 20 (14.4) | 29 (20.9) | 48 (34.5) | 32 (23) |
| Female                          | 53 (27.6)                      | 1 (1.9)     | 3 (5.7)   | 11 (20.8) | 30 (66)   | 8 (15.1) |
| Age                             |                                |             |         |         |         |         |
| < 55y                           | 89 (46.4)                      | 6 (6.7)     | 10 (11.2) | 17 (19.1) | 39 (43.8) | 17 (19.1) |
| ≥ 55y                           | 103 (53.6)                     | 5 (4.9)     | 13 (12.6) | 23 (22.3) | 39 (37.9) | 23 (22.3) |
| Location                        |                                |             |         |         |         |         |
| Esophagogastric junction        | 44 (22.9)                      | 1 (2.3)     | 4 (9.1)   | 8 (18.2)  | 20 (45.5) | 11 (25)  |
| Proximal gastric                | 71 (37)                        | 7 (9.9)     | 8 (11.3)  | 15 (21.1) | 23 (32.4) | 18 (25.4) |
| Distal gastric                  | 77 (40.1)                      | 3 (3.9)     | 11 (14.3) | 17 (22.1) | 35 (45.5) | 11 (14.3) |
| Maximal diameter of tumor bed   |                                |             |         |         |         |         |
| < 4.5 cm                        | 108 (56.2)                     | 9 (8.3)     | 20 (18.5) | 20 (18.5) | 44 (40.7) | 15 (139) |
| 4.5–8 cm                        | 64 (33.3)                      | 1 (1.6)     | 3 (4.7)   | 17 (266)  | 27 (422)  | 16 (25)  |
| > 8 cm                          | 20 (10.4)                      | 1 (5)       | 0 (0)     | 3 (15)    | 7 (35)    | 9 (45)   |
| Histological differentiation    |                                |             |         |         |         |         |
| Well-moderate                   | 45 (23.4)                      | 4 (8.9)     | 12 (26.7) | 9 (20)    | 16 (35.6) | 4 (8.9)  |
| Poor                            | 147 (76.6)                     | 7 (48)      | 11 (75)   | 31 (211)  | 62 (422)  | 36 (245) |
| Laurén classification           |                                |             |         |         |         |         |
| Intestinal                      | 77 (40.1)                      | 4 (5.2)     | 14 (18.2) | 14 (19.2) | 28 (36.4) | 15 (195) |
| Diffuse                         | 73 (38)                        | 7 (9.6)     | 5 (68)    | 10 (238)  | 33 (452)  | 14 (192) |
| Mixed                           | 42 (21.9)                      | 0 (0)       | 4 (9.5)   | 15 (357)  | 17 (40.5) | 11 (262) |
| LVI                             |                                |             |         |         |         |         |
| Negative                        | 94 (49)                        | 11 (11.7)   | 19 (20.2) | 28 (298)  | 26 (27.7) | 10 (106) |
| Positive                        | 98 (51)                        | 0 (0)       | 4 (41)    | 12 (122)  | 52 (53.1) | 30 (306) |
| PNI                             |                                |             |         |         |         |         |
| Negative                        | 76 (39.6)                      | 11 (14.5)   | 22 (28.9) | 13 (17.1) | 23 (303)  | 7 (9.2)  |
| Positive                        | 116 (60.4)                     | 0 (0)       | 1 (09)    | 27 (233)  | 55 (474)  | 33 (284) |
| AJCC ypT category               |                                |             |         |         |         |         |
| 0                               | 11 (5.7)                       | 11 (100)    | 0 (0)     | 0 (0)     | 0 (0)     | 0 (0)    |
| 1                               | 20 (10.4)                      | 0 (0)       | 12 (60)   | 5 (25)    | 3 (15)    | 0 (0)    |
| 2                               | 23 (12)                        | 0 (0)       | 5 (21.7)  | 6 (26.1)  | 12 (52.2) | 0 (0)    |
Table 2  Relationships between clinicopathological characteristics and pathological response evaluated by Mandard-TRG system (Continued)

|  | 57 (29.7) | 0 (0) | 5 (88) | 18 (31.6) | 25 (43.9) | 9 (15.8) |
| 4 | 81 (42.2) | 0 (0) | 1 (1.2) | 11 (13.6) | 38 (46.9) | 31 (38.3) |
| **AJCC ypN category** | **<0.001** |
| 0 | 55 (28.6) | 9 (16.4) | 13 (23.6) | 17 (30.9) | 10 (18.2) | 6 (10.9) |
| 1 | 36 (18.8) | 0 (0) | 6 (16.7) | 7 (194) | 16 (444) | 7 (194) |
| 2 | 50 (26) | 0 (0) | 3 (6) | 10 (20) | 32 (64) | 5 (10) |
| 3 | 51 (26.6) | 2 (3.9) | 1 (2) | 6 (11.8) | 20 (39.2) | 22 (43.1) |
| **AJCC stage** | **<0.001** |
| 0 | 9 (4.7) | 9 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 1 | 24 (12.5) | 0 (0) | 14 (58.3) | 7 (292) | 2 (8.3) | 1 (4.2) |
| 2 | 53 (27.6) | 2 (3.8) | 6 (11.3) | 14 (26.4) | 21 (396) | 10 (189) |
| 3 | 106 (55.2) | 0 (0) | 3 (2.8) | 19 (17.9) | 55 (519) | 29 (274) |
| **R0 resection** | **0.185** |
| Yes | 159 (82.8) | 11 (6.9) | 20 (12.6) | 35 (22) | 64 (403) | 29 (182) |
| No | 33 (17.2) | 0 (0) | 3 (9.1) | 5 (15.2) | 14 (424) | 11 (333) |
| **Adjuvant chemotherapy** | **0.766** |
| Not received | 59 (30.7) | 3 (5.1) | 6 (10.2) | 10 (169) | 25 (424) | 15 (254) |
| Received | 133 (69.3) | 8 (6) | 17 (12.8) | 30 (22.6) | 53 (398) | 25 (188) |
## Table 3 Relationships between clinicopathological characteristics and pathological response evaluated by JGCA-TRG system

| Characteristics                      | Total cases (n = 192), no. (%) | JGCA -TRG | 3 (n = 11), no. (%) | 2 (n = 63), no. (%) | 1b (n = 45), no. (%) | 1a (n = 33), no. (%) | 0 (n = 40), no. (%) | P value |
|--------------------------------------|--------------------------------|-----------|---------------------|---------------------|---------------------|---------------------|---------------------|---------|
| Gender                               |                                | 0.097     |                     |                     |                     |                     |                     |         |
| Male                                 | 139 (72.4)                     | 10 (7.2)  | 48 (34.5)           | 30 (21.6)           | 19 (13.7)           | 32 (23)            |                     |         |
| Female                               | 53 (27.6)                      | 1 (1.9)   | 15 (28.3)           | 15 (28.3)           | 14 (26.4)           | 8 (15.1)           |                     |         |
| Age                                  |                                | 0.711     |                     |                     |                     |                     |                     |         |
| < 55y                                | 89 (46.4)                      | 6 (6.7)   | 26 (29.2)           | 24 (27)             | 16 (18)             | 17 (19.1)          |                     |         |
| ≥ 55y                                | 103 (53.6)                     | 5 (4.9)   | 37 (35.9)           | 21 (20.4)           | 17 (16.5)           | 23 (22.3)          |                     |         |
| Location                              |                                | 0.287     |                     |                     |                     |                     |                     |         |
| Esophagogastric junction              | 44 (22.9)                      | 1 (2.3)   | 12 (27.3)           | 10 (22.7)           | 10 (22.7)           | 11 (25)            |                     |         |
| Proximal gastric                      | 71 (37)                        | 7 (9.9)   | 23 (32.4)           | 15 (21.1)           | 8 (11.3)            | 18 (25.4)          |                     |         |
| Distal gastric                        | 77 (40.1)                      | 3 (3.9)   | 28 (36.4)           | 20 (26)             | 15 (19.5)           | 11 (14.3)          |                     |         |
| Maximal diameter of tumor bed        |                                | <0.001    |                     |                     |                     |                     |                     |         |
| < 4.5 cm                              | 108 (56.2)                     | 9 (8.3)   | 40 (37)             | 27 (25)             | 17 (15.7)           | 15 (13.9)          |                     |         |
| 4.5–8 cm                              | 64 (33.3)                      | 1 (1.6)   | 21 (32.8)           | 14 (21.9)           | 12 (18.8)           | 16 (25)            |                     |         |
| > 8 cm                                | 20 (10.4)                      | 1 (5)     | 2 (10)              | 4 (20)              | 4 (20)              | 9 (45)             |                     |         |
| Histological differentiation          |                                | 0.060     |                     |                     |                     |                     |                     |         |
| Well-moderate                         | 45 (23.4)                      | 4 (8.9)   | 21 (46.7)           | 10 (22.2)           | 6 (13.3)            | 4 (8.9)            |                     |         |
| Poor                                  | 147 (76.6)                     | 7 (4.8)   | 42 (28.6)           | 35 (23.8)           | 27 (18.4)           | 36 (24.5)          |                     |         |
| Laurén classification                 |                                |           |                     |                     |                     |                     |                     |         |
| Intestinal                            | 77 (40.1)                      | 4 (5.2)   | 29 (37.7)           | 18 (23.4)           | 11 (14.3)           | 15 (19.5)          |                     |         |
| Diffuse                               | 73 (38)                        | 7 (9.6)   | 20 (27.4)           | 16 (21.9)           | 16 (21.9)           | 14 (19.2)          |                     |         |
| Mixed                                 | 42 (21.9)                      | 0 (0)     | 14 (33.3)           | 11 (26.2)           | 6 (14.3)            | 11 (26.2)          |                     |         |
| LVI                                   |                                | <0.001    |                     |                     |                     |                     |                     |         |
| Negative                              | 94 (49)                        | 11 (11.7) | 46 (48.9)           | 19 (20.2)           | 8 (8.5)             | 10 (10.6)          |                     |         |
| Positive                              | 98 (51)                        | 0 (0)     | 17 (17.3)           | 26 (26.5)           | 25 (25.5)           | 30 (30.6)          |                     |         |
| PNI                                   |                                | <0.001    |                     |                     |                     |                     |                     |         |
| Negative                              | 76 (39.6)                      | 11 (14.5) | 35 (46.1)           | 14 (18.4)           | 9 (11.8)            | 7 (9.2)            |                     |         |
| Positive                              | 116 (60.4)                     | 0 (0)     | 28 (24.1)           | 31 (26.7)           | 24 (20.7)           | 33 (28.4)          |                     |         |
| AJCC ypT category                     |                                | <0.001    |                     |                     |                     |                     |                     |         |
| 0                                     | 11 (5.7)                       | 11 (100)  | 0 (0)               | 0 (0)               | 0 (0)               | 0 (0)              |                     |         |
| 1                                     | 20 (10.4)                      | 0 (0)     | 17 (85)             | 1 (5)               | 2 (10)              | 0 (0)              |                     |         |
| 2                                     | 23 (12)                        | 0 (0)     | 11 (47.8)           | 6 (26.1)            | 6 (26.1)            | 0 (0)              |                     |         |
|  | 3 | 4 | 57 (29.7) | 0 (0) | 24 (42.1) | 16 (28.1) | 8 (14) | 9 (15.8) |
|  | 4 | 81 (42.2) | 0 (0) | 11 (13.6) | 22 (27.2) | 17 (21) | 31 (38.3) |
| AJCC ypN category | <0.001 | 0 | 55 (28.6) | 9 (16.4) | 30 (54.5) | 5 (9.1) | 5 (9.1) | 6 (10.9) |
| | 1 | 36 (18.8) | 0 (0) | 13 (26) | 11 (306) | 5 (13.9) | 7 (19.4) |
| | 2 | 50 (26) | 0 (0) | 13 (26) | 21 (42) | 11 (22) | 5 (10) |
| | 3 | 51 (266) | 2 (39) | 7 (13.7) | 8 (15.7) | 12 (23.5) | 22 (43.1) |
| AJCC stage | <0.001 | 0 | 9 (4.7) | 9 (100) | 0 (0) | 0 (0) | 0 (0) |
| | 1 | 24 (12.5) | 0 (0) | 21 (87.5) | 1 (4.2) | 1 (4.2) | 1 (4.2) |
| | 2 | 53 (27.6) | 2 (38) | 20 (37.7) | 12 (26) | 9 (17) | 10 (18.9) |
| | 3 | 106 (55.2) | 0 (0) | 22 (20.8) | 32 (302) | 23 (21.7) | 29 (27.4) |
| R0 resection | 0.046 | Yes | 159 (82.8) | 11 (69) | 55 (34.6) | 40 (25.2) | 24 (15.1) | 29 (18.2) |
| | No | 33 (17.2) | 0 (0) | 8 (24.2) | 5 (15.2) | 9 (27.3) | 11 (33.3) |
| Adjuvant chemotherapy | 0.676 | Not received | 59 (30.7) | 3 (5.1) | 16 (27.1) | 13 (22) | 12 (20.3) | 15 (25.4) |
| | Received | 133 (69.3) | 8 (6) | 47 (35.3) | 32 (24.1) | 21 (15.8) | 25 (18.8) |
### Table 4: Relationships between clinicopathological characteristics and pathological response evaluated by CAP-TRG system

| Characteristics                  | Total cases (n=192), no. (%) | CAP-TrG | P value |
|----------------------------------|-----------------------------|---------|---------|
| Gender                           |                             |         |         |
| Male                             | 139 (72.4)                  |         |         |
| Female                           | 53 (27.6)                   |         |         |
| Age                              |                             |         |         |
| < 55y                            | 89 (46.4)                   |         |         |
| ≥ 55y                            | 103 (53.6)                  |         |         |
| Location                         |                             |         |         |
| Esophagogastric junction         | 44 (22.9)                   |         |         |
| Proximal gastric                 | 71 (37)                     |         |         |
| Distal gastric                   | 77 (40.1)                   |         |         |
| Maximal diameter of tumor bed    |                             |         |         |
| < 4.5 cm                         | 108 (56.2)                  |         |         |
| 4.5 – 8 cm                       | 64 (33.3)                   |         |         |
| > 8 cm                           | 10 (5.2)                    |         |         |
| Histological differentiation     |                             |         |         |
| Well-moderate                    | 45 (23.4)                   |         |         |
| Poor                             | 147 (76.6)                  |         |         |
| Laurén classification            |                             |         |         |
| Intestinal                      | 77 (40.1)                   |         |         |
| Diffuse                          | 73 (38)                     |         |         |
| Mixed                            | 42 (21.9)                   |         |         |
| LVI                              |                             |         |         |
| Negative                         | 94 (49)                     |         |         |
| Positive                         | 98 (51)                     |         |         |
| PNI                              |                             |         |         |
| Negative                         | 116 (60.4)                  |         |         |
| Positive                         | 60 (29.6)                   |         |         |
| AJCC ypT category                |                             |         |         |
| 0                                | 11 (5.7)                    |         |         |
| 1                                | 111 (57.8)                  |         |         |
| 2                                | 110 (57.8)                  |         |         |
|     |         |         |         |         |         |
|-----|---------|---------|---------|---------|---------|
| 3   | 57 (29.7)| 0 (0)   | 5 (8.8) | 18 (31.6)| 34 (59.6)|
| 4   | 81 (42.2)| 0 (0)   | 1 (1.2) | 11 (13.6)| 69 (85.2)|

**AJCC ypN category**

|     |         |         |         |         |         |
|-----|---------|---------|---------|---------|---------|
| 0   | 55 (28.6)| 9 (16.4)| 13 (23.6)| 17 (30.9)| 16 (29.1)|
| 1   | 36 (18.8)| 0 (0)   | 6 (16.7) | 7 (19.4) | 23 (63.9)|
| 2   | 50 (26)  | 0 (0)   | 3 (6)    | 10 (20)  | 37 (74)  |
| 3   | 51 (26.6)| 2 (3.9) | 1 (2)    | 6 (11.8) | 42 (82.4)|

**AJCC stage**

|     |         |         |         |         |         |
|-----|---------|---------|---------|---------|---------|
| 0   | 9 (4.7) | 9 (100) | 0 (0)   | 0 (0)   | 0 (0)   |
| 1   | 24 (12.5)| 0 (0)   | 14 (58.3)| 7 (29.2)| 3 (12.5)|
| 2   | 53 (276)| 2 (3.8) | 6 (11.3) | 14 (26.4)| 31 (58.5)|
| 3   | 106 (552)| 0 (0)   | 3 (2.8)  | 19 (179) | 84 (79.2)|

**R0 resection**

|     |         |         |         |         |         |
|-----|---------|---------|---------|---------|---------|
| Yes | 159 (82.8)| 11 (6.9)| 20 (12.6)| 35 (22) | 93 (58.5)|
| No  | 33 (17.2)| 0 (0)   | 3 (9.1)  | 5 (15.2) | 25 (75.8)|

**Adjuvant chemotherapy**

|     |         |         |         |         |         |
|-----|---------|---------|---------|---------|---------|
| Not received | 59 (30.7)| 3 (5.1) | 6 (10.2) | 10 (169) | 40 (67.8)|
| Received    | 133 (693)| 8 (6)   | 17 (35.3)| 30 (226) | 78 (58.6)|

<0.001
Table 5  Relationships between clinicopathological characteristics and pathological response evaluated by China-TRG system

| Characteristics               | Total cases (n = 192), no. (%) | China-TRG |  |  |  |  |
|------------------------------|--------------------------------|-----------|---|---|---|---|
|                              |                                | Severe response (n = 34), no. (%) | Moderate response (n = 57), no. (%) | Mild response (n = 101), no. (%) |  |  |
| Gender                       |                                |  |  |  |  |  |  |
| Male                         | 139 (72.4)                     | 30 (21.6) | 41 (29.5) | 68 (48.9) | 0.063 |  |
| Female                       | 53 (27.6)                      | 4 (7.5)   | 16 (30.2) | 33 (62.3) |  |  |
| Age                          |                                |  |  |  |  |  |  |
| < 55y                        | 89 (46.4)                      | 15 (16.9) | 25 (28.1) | 49 (55.1) | 0.820 |  |
| ≥ 55y                        | 103 (53.6)                     | 19 (18.4) | 32 (31.1) | 52 (50.5) |  |  |
| Location                     |                                |  |  |  |  |  |  |
| Esophagogastric junction     | 44 (22.9)                      | 6 (13.6)  | 14 (31.8) | 24 (54.5) | 0.906 |  |
| Proximal gastric             | 71 (37)                        | 14 (19.7) | 22 (31)   | 35 (49.3) |  |  |
| Distal gastric               | 77 (40.1)                      | 14 (18.2) | 21 (27.3) | 42 (54.5) |  |  |
| Maximal diameter of tumor bed|                                |  |  |  |  | <0.001 |  |
| < 4.5 cm                     | 108 (56.2)                     | 28 (25.9) | 32 (29.6) | 48 (44.4) |  |  |
| 4.5–8 cm                     | 64 (33.3)                      | 5 (7.8)   | 21 (32.8) | 38 (59.4) |  |  |
| > 8 cm                       | 20 (10.4)                      | 1 (5)     | 4 (20)    | 15 (75)   |  |  |
| Histological differentiation |                                |  |  |  |  | 0.001 |  |
| Well-moderate                | 45 (23.4)                      | 16 (35.6) | 12 (26.7) | 17 (37.8) |  |  |
| Poor                         | 147 (76.6)                     | 18 (12.2) | 45 (30.6) | 84 (57.1) |  |  |
| Laurén classification        |                                |  |  |  |  | 0.264 |  |
| Intestinal                   | 77 (40.1)                      | 18 (23.4) | 22 (28.6) | 37 (48.1) |  |  |
| Diffuse                      | 73 (38)                        | 13 (17.8) | 20 (27.4) | 40 (54.8) |  |  |
| Mixed                        | 42 (21.9)                      | 3 (7.1)   | 15 (35.7) | 24 (57.1) |  |  |
| LVI                          |                                |  |  |  |  | <0.001 |  |
| Negative                     | 94 (49)                        | 30 (31.9) | 35 (37.2) | 29 (30.9) |  |  |
| Positive                     | 98 (51)                        | 4 (4.1)   | 22 (22.4) | 72 (73.5) |  |  |
| PNI                          |                                |  |  |  |  | <0.001 |  |
| Negative                     | 76 (39.6)                      | 33 (43.4) | 20 (26.3) | 23 (30.3) |  |  |
| Positive                     | 116 (60.4)                     | 1 (0.9)   | 37 (31.9) | 78 (67.2) |  |  |
| AJCC ypT category            |                                |  |  |  |  | <0.001 |  |
| 0                            | 11 (5.7)                       | 11 (100)  | 0 (0)     | 0 (0)     |  |  |
| 1                            | 20 (10.4)                      | 12 (60)   | 5 (25)    | 3 (15)    |  |  |
| 2                            | 23 (12)                        | 5 (21.7)  | 8 (34.8)  | 10 (43.5) |  |  |
| 3                            | 57 (29.7)                      | 5 (8.8)   | 26 (45.6) | 26 (45.6) |  |  |
| 4                            | 81 (42.2)                      | 1 (1.2)   | 18 (22.2) | 62 (76.5) |  |  |
| AJCC ypN category            |                                |  |  |  |  | <0.001 |  |
| 0                            | 55 (28.6)                      | 22 (40)   | 18 (32.7) | 15 (27.3) |  |  |
| 1                            | 36 (18.8)                      | 5 (13.9)  | 12 (33.3) | 19 (52.8) |  |  |
| 2                            | 50 (26)                        | 4 (13.9)  | 19 (38)   | 27 (54)   |  |  |
| 3                            | 51 (26.6)                      | 3 (5.9)   | 8 (15.7)  | 40 (78.4) |  |  |
| AJCC stage                   |                                |  |  |  |  | <0.001 |  |
| 0                            | 9 (4.7)                        | 9 (100)   | 0 (0)     | 0 (0)     |  |  |
| 1                            | 24 (12.5)                      | 14 (58.3) | 7 (29.2)  | 3 (12.5)  |  |  |
Table 5 Relationships between clinicopathological characteristics and pathological response evaluated by China-TRG system (Continued)

| Grade | No Response | Partial Response | Severe Response |
|-------|-------------|------------------|-----------------|
| 2     | 52 (27.6)   | 7 (13.2)         | 17 (32.1)       |
| 3     | 106 (55.2)  | 4 (3.8)          | 33 (31.1)       |

R0 resection

| Yes   | 159 (82.8)  | 31 (19.5) | 49 (30.8) | 79 (49.7) |
| No    | 33 (17.2)   | 3 (9.1)   | 7 (21.2)  | 23 (69.7) |

Adjuvant chemotherapy

| Not received | 59 (30.7) | 10 (16.9) | 17 (28.8) | 32 (54.2) |
| Received     | 133 (69.3)| 24 (18)   | 39 (29.3) | 70 (52.6) |

The relationships between clinicopathological characteristics and pathological response evaluated by China-TRG system showed significant correlations (Table 5).

Discussion

Neoadjuvant and adjuvant therapy have been applied to improve the outcome of localized advanced GC, especially in east Asia [11]. Preoperative therapy promoted R0 resection rates in some randomized studies [12]. Although the efficacy of preoperative chemotherapy could be partially reflected by the Response Evaluation Criteria in Solid Tumors (RECIST), RECIST is not always consistent with histopathological regression and prognosis. Thus the relationship among histopathological tumor regression evaluation, efficiency of the multimodality
| Characteristics                  | Total cases (n = 192), no. (%) | Becker-TRG |   |   |   |   | P value |
|----------------------------------|-------------------------------|------------|---|---|---|---|---------|
|                                 |                               | 1a (n = 11), no. (%) | 1b (n = 23), no. (%) | 2 (n = 67), no. (%) | 3 (n = 91), no. (%) |   |
| Gender                          |                               |             |   |   |   |   | 0.142   |
| Male                            | 139 (72.4)                     | 10 (72)    | 20 (14.4) | 45 (32.4) | 64 (46) |   |
| Female                          | 53 (27.6)                      | 1 (19)     | 3 (5.7)   | 22 (41.5) | 27 (50.9) |   |
| Age                             |                               |             |   |   |   |   | 0.945   |
| < 55y                           | 89 (46.4)                      | 6 (6.7)    | 10 (11.2) | 31 (34.8) | 42 (47.2) |   |
| ≥ 55y                           | 103 (53.6)                     | 5 (4.9)    | 13 (12.6) | 36 (35)   | 49 (47.6) |   |
| Location                        |                               |             |   |   |   |   | 0.562   |
| Esophagogastric junction        | 44 (22.9)                      | 1 (2.3)    | 4 (9.1)   | 15 (34.1) | 24 (54.5) |   |
| Proximal gastric                | 71 (37)                        | 7 (9.9)    | 8 (11.3)  | 24 (33.8) | 32 (45.1) |   |
| Distal gastric                  | 77 (40.1)                      | 3 (3.9)    | 11 (14.3) | 28 (36.4) | 35 (45.5) |   |
| Maximal diameter of tumor bed   |                               |             |   |   |   |   | 0.003   |
| < 4.5 cm                        | 108 (56.2)                     | 9 (8.3)    | 20 (18.5) | 35 (32.4) | 44 (40.7) |   |
| 4.5–8 cm                        | 64 (33.3)                      | 1 (1.6)    | 3 (4.7)   | 28 (43.8) | 32 (50)   |   |
| > 8 cm                          | 20 (10.4)                      | 1 (5)      | 0 (0)     | 4 (20)    | 15 (75)   |   |
| Histological differentiation    |                               |             |   |   |   |   | 0.003   |
| Well-moderate                   | 45 (23.4)                      | 4 (8.9)    | 12 (26.7) | 14 (31.1) | 15 (33.3) |   |
| Poor                            | 147 (76.6)                     | 7 (48)     | 11 (7.5)  | 53 (36.1) | 76 (51.7) |   |
| Laurén classification           |                               |             |   |   |   |   | 0.127   |
| Intestinal                      | 77 (40.1)                      | 4 (5.2)    | 14 (18.2) | 25 (32.5) | 34 (44.2) |   |
| Diffuse                         | 73 (38)                        | 7 (9.6)    | 5 (6.8)   | 24 (32.9) | 37 (50.7) |   |
| Mixed                           | 42 (21.9)                      | 0 (0)      | 4 (9.5)   | 18 (42.9) | 20 (47.6) |   |
| LVI                             |                               |             |   |   |   |   | <0.001  |
| Negative                        | 94 (49)                        | 11 (11.7)  | 19 (20.2) | 39 (41.5) | 25 (26.6) |   |
| Positive                        | 98 (51)                        | 0 (0)      | 4 (4.1)   | 28 (28.6) | 66 (67.3) |   |
| PNI                             |                               |             |   |   |   |   | <0.001  |
| Negative                        | 76 (39.6)                      | 11 (14.5)  | 22 (28.9) | 22 (28.9) | 21 (27.6) |   |
| Positive                        | 116 (60.4)                     | 0 (0)      | 1 (0.9)   | 45 (38.8) | 70 (60.3) |   |
| AJCC ypT category               |                               |             |   |   |   |   | <0.001  |
| 0                               | 11 (5.7)                       | 11 (100)   | 0 (0)     | 0 (0)     | 0 (0)     |   |
| 1                               | 20 (10.4)                      | 0 (0)      | 12 (60)   | 5 (25)    | 3 (15)    |   |
| 2                               | 23 (12)                        | 0 (0)      | 5 (21.7)  | 10 (43.5) | 8 (34.8)  |   |
Table 6  Relationships between clinicopathological characteristics and pathological response evaluated by Becker-TRG system (Continued)

|        | TRG 1 | TRG 2 | TRG 3 | TRG 4 | TRG 5 |
|--------|-------|-------|-------|-------|-------|
|        | 0     | 1     | 2     | 3     |
| AJCC ypN category |       |       |       |       |       |
| 0      | 55 (28.6) | 9 (16.4) | 13 (23.6) | 19 (34.5) | 14 (25.5) |
| 1      | 36 (18.8) | 0 (0)   | 6 (16.7)  | 16 (44.4) | 14 (38.9) |
| 2      | 50 (26)   | 0 (0)   | 3 (6)    | 21 (42)   | 26 (52)   |
| 3      | 51 (26.6) | 2 (3.9) | 1 (2)    | 11 (21.6) | 37 (72.5) |
| AJCC stage |       |       |       |       |       |
| 0      | 9 (4.7)   | 9 (100) | 0 (0)   | 0 (0)    | 0 (0)    |
| 1      | 24 (12.5) | 0 (0)   | 14 (58.3) | 7 (29.2) | 3 (12.5) |
| 2      | 53 (27.6) | 2 (3.8) | 6 (11.3) | 21 (39.6) | 24 (45.3) |
| 3      | 106 (55.2)| 0 (0)   | 3 (2.8)  | 39 (36.8) | 64 (60.4) |
| R0 resection |       |       |       |       |       |
| Yes    | 159 (82.8)| 11 (69) | 20 (12.6) | 57 (35.8) | 71 (44.7) |
| No     | 33 (17.2) | 0 (0)   | 3 (9.1)  | 10 (30.3) | 20 (60.6) |
| Adjuvant chemotherapy |       |       |       |       |       |
| Not received | 59 (30.7) | 3 (5.1) | 6 (10.2) | 20 (33.9) | 30 (50.8) |
| Received | 133 (69.3)| 8 (6)   | 17 (35.3) | 47 (35.3) | 61 (45.9) |
| Characteristics                  | OS HR | 95% CI       | P value | PFS HR | 95% CI       | P value |
|---------------------------------|-------|--------------|---------|--------|--------------|---------|
| **Gender**                      |       |              |         |        |              |         |
| Male (reference)                | 1     | 1            |         |        |              |         |
| Female                          | 1.179 | 0.740–1.876  | 0.488   | 1.309  | 0.859–1.994  | 0.211   |
| **Age**                         |       |              |         |        |              |         |
| <55y (reference)                | 1     | 1            |         |        |              |         |
| ≥55y                            | 1.120 | 0.903–1.390  | 0.303   | 0.856  | 0.577–1.270  | 0.441   |
| **Location**                    |       |              |         |        |              |         |
| Esophagogastric junction (ref.) | 1     | 1            |         |        |              |         |
| Proximal gastric                | 0.952 | 0.555–1.632  | 0.857   | 0.829  | 0.506–1.358  | 0.456   |
| Distal gastric                  | 0.634 | 0.360–1.117  | 0.115   | 0.631  | 0.380–1.046  | 0.074   |
| Maximal diameter of tumor bed   | 1.712 | 1.275–2.999  | <0.001  | 1.709  | 1.304–2.239  | <0.001  |
| Histological differentiation    | 3.057 | 1.617–5.782  | 0.001   | 2.667  | 1.513–4.699  | 0.001   |
| Laurén classification           |       |              |         |        |              |         |
| Intestinal (reference)          | 1     | 1            |         |        |              |         |
| Diffuse                         | 2.228 | 1.339–3.709  | 0.002   | 1.896  | 1.199–2.999  | 0.006   |
| Mixed                           | 2.206 | 1.216–4.003  | 0.009   | 1.911  | 1.113–3.280  | 0.019   |
| LVI                             | 3.318 | 2.089–5.270  | <0.001  | 3.324  | 2.180–5.069  | <0.001  |
| PNI                             | 2.878 | 1.750–4.733  | <0.001  | 2.724  | 1.737–4.271  | <0.001  |
| AJCC ypT category               | 1.876 | 1.457–2.415  | <0.001  | 1.739  | 1.396–2.168  | <0.001  |
| AJCC ypN category               | 1.946 | 1.572–2.408  | <0.001  | 1.918  | 1.578–2.330  | <0.001  |
| AJCC stage                      | 2.484 | 1.724–3.580  | <0.001  | 2.270  | 1.650–3.122  | <0.001  |
| Mandard-TRG                     |       |              |         |        |              |         |
| 1 (reference)                   |       | 1            |         |        |              |         |
| 2                               | 0.98  | 0.244–3.929  | 0.977   | 1.293  | 0.343–4.877  | 0.704   |
| 3                               | 1.956 | 0.568–6.730  | 0.287   | 2.143  | 0.631–7.283  | 0.222   |
| 4                               | 2.717 | 0.836–8.831  | 0.096   | 3.155  | 0.979–10.168 | 0.054   |
| 5                               | 3.682 | 1.094–12.394 | 0.035   | 4.570  | 1.380–15.132 | 0.013   |
| JGCA-TRG                        |       |              |         |        |              |         |
| 3 (reference)                   |       | 1            |         |        |              |         |
| 2                               | 1.531 | 0.457–5.126  | 0.49    | 1.782  | 0.539–5.892  | 0.344   |
| 1b                              | 2.626 | 0.781–8.831  | 0.119   | 2.621  | 0.786–8.738  | 0.117   |
| 1a                              | 2.875 | 0.836–9.884  | 0.094   | 4.022  | 1.199–13.491 | 0.024   |
| 0                               | 3.676 | 1.092–12.371 | 0.035   | 4.556  | 1.376–15.085 | 0.013   |
| CAP-TRG                         |       |              |         |        |              |         |
| 0 (reference)                   |       | 1            |         |        |              |         |
| 1                               | 0.979 | 0.244–3.927  | 0.977   | 1.292  | 0.343–4.873  | 0.705   |
| 2                               | 1.953 | 0.568–6.719  | 0.288   | 2.140  | 0.630–7.272  | 0.223   |
| 3                               | 2.996 | 0.937–9.586  | 0.064   | 3.558  | 1.119–11.311 | 0.032   |
| China-TRG                       |       |              |         |        |              |         |
| Severe response (reference)     |       | 1            |         |        |              |         |
| Moderate response               | 1.719 | 0.808–3.657  | 0.160   | 1.661  | 0.834–3.308  | 0.149   |
| Mild response                   | 2.856 | 1.450–5.628  | 0.002   | 2.868  | 1.544–5.328  | 0.001   |
therapy and prognosis requires further illumination. Globally, there have been many kinds of histopathological tumor regression grading systems. Mandard et al. first published their five-tiered TRG system for esophageal carcinoma in 1994. It was reproducible and used widely in carcinomas of esophagus/esophagogastric junction and rectum, but there have been no published applications in GC yet. CAP recommended a simplified four-tiered TRG system based on Mandard-TRG system. In China, a three-tiered grading system is used to assess therapeutic response for solid malignancies. However, its applicability on GC remained unclear. Becker et al. proposed a semi-quantitative four-tiered TRG system in 2003, and then they proved the applicability on GC in 2011. In Japan, the wildly used method to evaluate pathological response is JGCA-TRG, of which the criteria for tumor regression separation are quite distinct from the other four TRG systems.

In this study, 118 (61.4%) patients had mild or minimal tumor regression. Only 11 (5.7%) cases got complete regression without any residual tumor cells on the primary sites, but unfortunately 2 of them were found with residual lymph nodes metastasis, probably resulting in poor outcomes. Twenty-three (12.0%) patients had nearly complete regression with a few residual tumor cells. We supposed the patients

| Table 7 Univariate Cox regression analyses (Continued) |
|------------------------------------------|
| Becker-TRG                               |
| 1a (reference)                           |
| 1b                                        |
| 2                                         |
| 3                                         |
| R0 resection                              |
| Yes (reference)                           |
| No                                        |
| Adjuvant chemotherapy                     |
| Not received (reference)                  |
| Received                                 |

|                                | 1a (reference) | 1b | 2    | 3    |
|--------------------------------|----------------|----|------|------|
| 1a (reference)                 | 1              |    |      |      |
| 1b                            | 0.980          | 0.244–3.927 | 0.977 | 1.292 | 0.343–4.872 | 0.705 |
| 2                              | 2.216          | 0.673–7.294 | 0.190 | 2.295 | 0.702–7.502 | 0.169 |
| 3                              | 3.109          | 0.964–10.028 | 0.058 | 3.964 | 1.239–12.681 | 0.020 |

|                                | 1a (reference) | 1b | 2    | 3    |
|--------------------------------|----------------|----|------|------|
| R0 resection                   | 1              |    |      |      |
| Yes (reference)                | 3.382          | 2.022–5.659 | <0.001 | 3.656 | 2.315–5.774 | <0.001 |
| No                             | 1.040          | 0.633–1.707 | 0.878 | 1.227 | 0.774–1.943 | 0.384 |

Fig. 1 Overall survival curves of five TRG systems, respectively. a Mandard-TRG, b JGCA-TRG, c CAP-TRG, d China-TRG and e Becker-TRG

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who reached complete response should have a better prognosis while the patients who reached nearly complete response should have a worse prognosis. However the actual results did not confirm this. Agoston et al. defined pathological complete response as neither residual primary tumor nor residual lymph node metastasis existing [13]. They reviewed esophageal adenocarcinoma 93 cases with complete response and found that adequacy of histological examination of the tumor bed affected the prognosis. In our study, the number of tumor blocks ranged from 4 to 53 in the complete response cases, while the number ranged from 5 to 77 in the nearly complete response cases. The fewer blocks of some cases might indicate potentially insufficient tumor sampling. Meanwhile, in some other studies which emphasized on adequacy of gross sampling, the percentage of complete response in GC ranged from 1.2 to 3.6% [14–16]. Among the 23 nearly complete response cases in our study, only 5 were classified to postsurgical T3 or T4 categories, while the others were suspected to have earlier T categories before the preoperative therapy. This could be supposed to explain the different prognosis between patients who reached complete response and the patients who had nearly complete response. It is controversial on whether separating the complete response from the nearly complete response. Becker et al. separated the complete response category from the nearly complete response category and assessed separately, however, they combined them for survival analysis [9].

Chirieac et al. demonstrated their TRG system as an independent predictor on esophageal and esophagogastric junction cancer. They evaluated the residual tumor semi-quantitatively as 0% residue, 1–50% residue and >50% residue [17]. Becker et al. found the significance in multivariate analysis on the proportion

![Fig. 2](image.png) Progression-free survival curves of five TRG systems, respectively. a Mandard-TRG, b JGCA-TRG, c CAP-TRG, d China-TRG and e Becker-TRG

| Table 8 Multivariate Cox regression analyses |
|---------------------------------------------|
| Characteristics | OS | | | PFS | | |
| | HR | 95% CI | P value | HR | 95% CI | P value |
| Histological differentiation | - | - | - | 1.662 | 0.914–3.022 | 0.096 |
| LVI | 1.651 | 0.976–2.793 | 0.062 | 1.766 | 1.091–2.861 | 0.021 |
| AJCC ypT category | 1.355 | 1.029–1.784 | 0.031 | - | - | - |
| AJCC ypN category | 1.487 | 1.168–1.894 | 0.001 | 1.479 | 1.180–1.855 | <0.001 |
| R0 resection | 2.386 | 1.398–4.073 | 0.001 | 2.457 | 1.516–3.985 | <0.001 |
of residual tumor between <10 and >10% in GC [9]. Both studies were based on large number of patients and long-term follow-up. On contrary, more studies did not demonstrate the independent role of TRG for prognosis. In our univariate survival analysis, all the five TRG systems showed statistical significance which was coincident with other studies [12, 14, 18, 19]. We collected exhaustive clinicopathological characteristics to establish the reliability of this study. The results indicated that all the TRG systems tightly correlated with LVI, postsurgical T and N categories, therefore the staging status and LVI would affect the statistical significance of the TRG systems in multivariate survival analysis. This could elucidate the absence of independent significance of the TRG systems. As compared with other grading systems, the hazard ratio of no/slightly response grade in both Mandard-TRG system and JGCA-TRG system revealed higher hazard of death and disease progression than that of severe response grade when using univariate Cox survival analysis. Furthermore, the main difference between the two five-tiered TRG systems is whether separating the category of nearly complete response from partial response. In Mandard-TRG system, the category of nearly complete response is separated, however, in JGCA-TRG system, it is not. Because the median survival time of patients with nearly complete response in Mandard-TRG system (84.4 months) was much longer than those with partial response in JGCA-TRG (57.8 months) (Table 9), separation of nearly complete response and partial response categories in Mandard-TRG system could be more reasonable for prognosis prediction.

### Conclusions

This study analyzed five classic TRG systems on GC after neoadjuvant chemotherapy and revealed the significance of all the five TRG systems in univariate survival analysis. We recommend Mandard-TRG system in GC evaluation for prediction of survival.

### Abbreviations

AJCC: American Joint Committee on Cancer; CAP: College of American Pathologists; GC: Gastric cancer; JGCA: The Japanese Gastric Cancer Association; LVI: Lymph-vascular invasion; OS: Overall-survival; PFS: Progression-free-survival; PNI: Perineural invasion; RECIST: Response Evaluation Criteria in Solid Tumors; TRG: Tumor regression grading.

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### Availability of data and materials

The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Authors’ contributions

LX and LY designed this study. YS and YZ enrolled patients and collected clinical data. YZ, JY and LX evaluated pathological sections. LX, YJ, SH, XX and YZ conducted statistical analysis. The manuscript was drafted by YZ, YS, JY and reviewed for content by LX, XX, SH and YJ. All authors read and approved the final manuscript.

### Competing interests

The authors declare that they have no competing interests.

### Consent for publication

Not applicable.

### Ethics approval and consent to participate

This study was conducted after approval by the Independent Ethics Committee from National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. NCC2013RE-049). The consent was not required from each patient because this is a retrospective study. All procedures were performed in line with the declaration of Helsinki’s version of 1983.

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### Table 9 Comparison of median survival time between Mandard-TRG and JGCA-TRG

| TRG systems | Median for survival time |
|-------------|-------------------------|
|             | OS                     | PFS           |
| Mandard-TRG |                        |               |
| 1           | Not reached             | Not reached   |
| 2           | 84.4                    | Not reached   |
| 3           | 51.8                    | 42.4          |
| 4           | 38.7                    | 22.1          |
| 5           | 24.3                    | 12.8          |
| JGCA-TRG    |                        |               |
| 3           | Not reached             | Not reached   |
| 2           | 57.8                    | 51.8          |
| 1b          | 38.7                    | 29.3          |
| 1a          | 30.8                    | 9.6           |
| 0           | 24.3                    | 12.8          |
