Clinicopathological characteristics and survival outcomes of younger patients with gastric cancer: a systematic review and meta-analysis

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Background: Survival outcomes of gastric cancer in younger patients have been reported in several studies with controversial results. This systematic review and meta-analysis investigated the clinicopathological characteristics, postoperative complications, and survival outcomes between younger and older patients.

Methods: We systematically reviewed clinical researches from PubMed, The Cochrane Library, Embase, and Web of science published up to December 2019. The effect size for the included studies was estimated with the odds ratio (OR). Heterogeneity was investigated using the $\chi^2$ test and $I^2$ test, while sensitivity analyses were performed to identify the source of substantial heterogeneity.

Results: A total of 25 clinical studies involving 81,188 gastric cancer patients were included in this meta-analysis, of which one was a prospective study. Younger patients were more likely to be females, pTNM stage IV and peritoneal metastasis. The incidence of postoperative complications, lymph node metastasis, as well as hepatic metastasis of younger patients was significantly lower than that of the older. There was no statistical difference in overall survival (OS) between the younger and older patients with gastric cancer. After stratification for patients with gastrectomy, however, younger patients were associated with a better 5-year OS relative to older patients.

Conclusions: In conclusion, younger patients with gastric cancer were more often diagnosed as poorly differentiation and later pTNM tumor stage. However, younger cancer patients following gastrectomy had a better OS rate than patients in older group. Future large-scale analyses are expected to confirm our findings.

Keywords: Gastric cancer; younger adult; clinicopathological characteristics; survival outcomes; meta-analysis

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Introduction

Gastric cancer is an aggressive malignancy and remains the third leading cause of cancer-related death worldwide (1,2). Although the overall incidence of gastric cancer showed a decline worldwide, younger cancer patients had increased obviously during the last decades (3). The growing incidence, as well as its aggressive biological behavior as reported (4,5), has renewed interest in the surgery-based management of younger gastric cancer patients with a focus on therapeutic strategies.
To date, the survival outcomes of younger patients were still controversial. Previous data reported that younger patients had worse survival rates than older (6-9), whereas several studies showed a similar prognosis (10-20). Some studies even expressed that younger patients were associated with improved survival outcomes (21-30). A significant reason for these inconsistent findings from published studies was the different age cutoffs on defining younger patients (6,7,29,30). A published meta-analysis has reported improved 5-year survival in the younger group. However, it was primarily limited to the small sample size and significant heterogeneity (31). Besides, there was currently no randomized clinical trial that targeted the issue.

As such, our study aimed to compare the clinicopathological characteristics, postoperative complications, as well as survival outcomes between younger and older patients with gastric cancer through systematic review and meta-analysis, thus providing evidence for the development of guiding strategies for younger gastric cancer patients. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/tcr-20-2024).

Methods

Search strategy

Clinical studies were systematically searched from PubMed, Web of Science, Embase, and The Cochrane Library. The following fields were used for the search: “gastric” or “stomach,” “cancer” or “carcinoma” or “neoplasm” or “tumor,” “young adult” or “younger” or “youth.” These searches were limited to clinical articles published up to December 2019.

Inclusion and exclusion criteria

Studies met the following criteria were included: (I) researches compared gastric cancer in the younger group (≤40 years of age) and older group (>40 years of age); (II) analyses contained quantitative clinicopathological information; (III) researches involved at least one of the mentioned survival outcomes.

Studies were excluded from the analysis as follow: (I) publications were position papers, editorials, case reports, comments, or review articles; (II) literature duplication based on an author or center; (III) research data was inappropriate or cannot be extracted; (IV) studies lacked control group for meta-analysis.

Data extraction

Two independent reviewers extracted predesigned data from the included studies. The extracted information was as follows: Basic characteristics of the study, including authors, country, patient inclusion criteria, sample size, design as well as quality assessment; Clinicopathological characteristics of patients, including gender, tumor location, differentiation, Lauren type, Borrmann classification, \( p\)TNM stage, and therapeutic regimens (involving chemotherapy, total/subtotal gastrectomy, curative resection, and lymphadenectomy); Survival outcomes, including metastasis, recurrence, and the short or long-term survival rates on different clinical tumor stage. The stage of gastric cancer was based on the American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) staging system. Lymphadenectomy was divided into D1 to D4, depending on the primary tumor location and removal of each lymph node station (32). Gastrectomy was defined as patients received surgery with or without D2 lymphadenectomy, while curative gastrectomy was defined as resection with D2 lymphadenectomy and a negative margin. The disagreement was resolved through discussion among the reviewers.

Quality assessment

The quality of the included studies was evaluated using The Newcastle-Ottawa Quality Assessment Scale (NOS) (33). The NOS checklist consisted of three major categories (selection, comparability, and outcome) with a maximum of nine stars. Each included study achieving six or more number of stars was graded high quality. Any disagreement was discussed to reach a consensus.

Statistical analysis

We conducted the review and meta-analysis using Revman software, version 5.3 (Cochrane Collaboration, Oxford, United Kingdom). Categorical variables were analyzed by the odds ratio (OR), while the corresponding 95% confidence interval (CI) was recorded. The Z test was conducted to determine the OR, with \( P<0.05 \) considered statistical significance. Heterogeneity was investigated using the \( \chi^2 \) test and the \( I^2 \) test. If significant heterogeneity existed, we employed the random effect model; otherwise, the fixed
effects model was adopted (34,35). Sensitivity analyses were undertaken to investigate sources of substantial heterogeneity.

**Results**

**Studies selection**

Our initial search strategy generated a total of 8,686 relevant clinical studies. After a screening of titles and abstracts, 108 articles were scrutinized by a full-text review. Eighty-three studies were eventually excluded by following the exclusion criteria and inclusion criteria. In total, the eligible 25 clinical studies (4,5,8-30) involving 81,188 gastric cancer patients were entered into the review and meta-analysis, of which one was a prospective study (17), three were multicenter studies (16,19,21), and the rest were all retrospective studies. Figure 1 showed the flow chart of the search process. The NOS scores and essential characteristics of the eligible studies were shown in Table 1.

**Clinicopathological characteristics**

The clinicopathologic characteristics of the gastric cancer patients were presented in Tables 2 and S1. Compared with the older group, younger patients with gastric cancer were more often female from pooled 25 studies (OR =2.09, 95% CI: 1.81–2.41, P<0.001, I²=76%) (Figure S1). Younger patients were more likely to be a diffuse type (OR =4.29, 95% CI: 3.15–5.85, P<0.001, I²=82%), pTNM stage IV (OR =1.21, 95% CI: 1.08–1.35, P<0.001, I²=0), poorly differentiation (OR =3.59, 95% CI: 2.89–4.47, P<0.001, I²=82%), and a signet ring cell carcinoma (OR =4.81, 95% CI: 4.33–5.33, P<0.001, I²=0) (Figure S2).

Concerning to therapeutic regimen, six studies showed that younger group had a higher chemotherapy rate when compared to older group (OR =1.79, 95% CI: 1.49–2.16, P<0.001, I²=43%). In addition, the proportions of younger patients underwent subtotal gastrectomy or D1 resection were significantly lower than those of the older (OR =0.88, 95% CI: 0.79–0.99, P=0.03, I²=39%; OR =0.59, 95% CI: 0.48–0.73, P<0.001, I²=25%, respectively). However, there...
| Authors          | Country   | Patient criteria                                                                 | NOS | Group | Age | Gender | Tumor location | pTNM stage |
|-----------------|-----------|----------------------------------------------------------------------------------|-----|-------|-----|---------|---------------|------------|
| Song et al.     | China     | GC underwent surgery (2007–2011)                                                 | 7   | YG ≤40 | 112 | –      | 59 21 64      | 5 30 59 18 |
| Cormedi et al.  | Brazil    | GC (2011–2013)                                                                   | 8   | YG ≤40 | 71  | 37     | 34 61 208     | 25 89 206 38 |
| Tavares et al.  | Portugal  | GC with surgery (2000–2005)                                                     | 7   | YG ≤40 | 23  | –      | 12 64 18      | 4 5 23 36 |
| Guan et al.     | the United States | GC (1973–2014)                                                | 8   | YG <35 | 1,369 | –    | 728 338 133 275 | 51 59 119 385 |
| Isobe et al.    | Japan     | GAC (1977–2006)                                                                 | 8   | YG ≤35 | 169  | 34.5±4.8 | 34 79 90 40 | 68 30 23 48 |
| Kim et al.      | Korea     | GC (1986–2000)                                                                   | 8   | YG ≤35 | 137  | 30.6±5.1 | 63 74 50 56 | 41 21 36 39 |
| Kunisaki et al. | Japan     | GC underwent curative surgery (1985–1999)                                        | 8   | YG ≤35 | 131  | 35.2±5.0 | 64 67 44 19 | 79 16 24 12 |
| Liu et al.      | China     | GC underwent surgery; no chemotherapy; no metastasis. (2008–2014)              | 7   | YG ≤35 | 198  | –      | 115 83 56 26 | – – – – – |
| Okamoto et al.  | Japan     | GC underwent laparotomy (1960–1984)                                             | 6   | YG <30 | 34   | 24.9    | 10 3 13 7    | – – – – – |
| Takatsu et al.  | Japan     | GC underwent surgical resection (2000–2010)                                      | 8   | YG ≤30 | 136  | 36 [16–39] | 72 64 25 35 | 65 21 28 22 |
| Tekesin et al.  | Turkey    | GC (1990–2014)                                                                   | 7   | YG ≤30 | 92   | 36 [22–40] | 53 39 17 7   | 5 4 17 52 |
| Wang et al.     | China     | GC underwent gastrectomy (1998–2006)                                            | 7   | YG ≤30 | 21   | 34.9±1.1 | 9 12 7 25    | – – – – – |
|                |           |                                                                                  |     | YG >40 | 774  | 60 [41–75] | 553 221 141 121 | – – – – – |
|                |           |                                                                                  |     | YG >55 | 36   | 67.1±0.8 | 22 14 7 25    | 11 9 15 1 |
| Authors       | Country | Patient criteria                                      | Document type     | NOS | Group     | No. | Age | Gender | Tumor location | pTNM stage |
|--------------|---------|------------------------------------------------------|-------------------|-----|-----------|-----|-----|---------|----------------|------------|
| Hsieh et al. (18) | Japan   | GAC underwent curative gastrectomy (1981–1992)       | Retrospective Study | 7   | YG ≤40    | 115 | 34.1±4.1 | Male   | Upper | 68 | 23 | 22 | 56 | 14 |
|              |         |                                                      |                   |     | YG >60    | 1,009 | 626 | 373 | 194 160 626 | 293 | 160 | 467 | 89 |
| Ma et al. (19)  | China   | GC underwent curative surgery (2009–2011)            | Retrospective Study | 7   | YG ≤40    | 125 | 34.0 | Male   | Upper | 29 | 14 | 71 | – |
|              |         |                                                      |                   |     | YG >40    | 1,752 | 1,341 | 411 | –    | –    | 403 | 400 | 946 | – |
| Mitsudomi et al. (20) | Japan      | GC (1970–1984)                                       | Retrospective Study | 7   | YG ≤40    | 128 | 35.0 | Female | Upper | 58 | 31 | – | – |
|              |         |                                                      |                   |     | YG >50    | 1,275 | 863 | 412 | 131 379 550 | – | – | – | – |
| Kulig et al. (21) | Poland   | GC (1977–1998)                                       | Retrospective Study | 6   | YG ≤40    | 214 | 35.0 | Female | Upper | 56 | 59 | 31 | – |
|              |         |                                                      |                   |     | YG >40    | 3,217 | 2,277 | 940 | 387 733 677 | 315 | 251 | 380 | 770 |
| Bani-Hani et al. (22) | Jordan | GAC (1991–2001)                                       | Retrospective Study | 7   | YG ≤40    | 17  | 36.3±0.9 | Male   | Upper | 3 | 35 | 46 | 7 |
|              |         |                                                      |                   |     | YG >40    | 159  | 104 | 55 | 26 39 83 | 11 39 55 46 |
| Kim et al. (23) | Korea   | GC underwent surgery (1993–2000)                      | Retrospective Study | 7   | YG ≤40    | 175 | 34.58±4.26 | Male   | Upper | 75 | 67 | 83 | 79 | 20 | 49 | 37 |
|              |         |                                                      |                   |     | YG >40    | 1,124 | 765 | 359 | 120 364 624 | 439 | 145 | 304 | 236 |
| Lai et al. (24) | Korea   | GC underwent curative surgery (1987–2004)            | Retrospective Study | 8   | YG ≤40    | 883 | 476 | 407 | 125 | – | – | 444 | 135 | 213 | 91 |
|              |         |                                                      |                   |     | YG >40    | 6,071 | 4,195 | 1,876 | 720 | – | – | 2,850 | 1,057 | 1,567 | 597 |
| Maehara et al. (25) | Japan     | GC underwent surgery (1965–1991)                      | Retrospective Study | 6   | YG ≤40    | 174 | 38.8±4.9 | Male   | Upper | 85 | 31 | 63 | – | – | – | – |
|              |         |                                                      |                   |     | YG >70    | 356 | 247 | 109 | 90 86 152 | – | – | – | – |
| Silva et al. (26) | Brazil     | GAC (1988–2005)                                       | Retrospective Study | 7   | YG ≤40    | 62  | 38 | 24 | 9 | 50 | 21 | 35 | – |
|              |         |                                                      |                   |     | YG >40    | 453 | 288 | 165 | 68 | 385 | 127 | 280 | – |
| Zhou et al. (27) | China   | GC resections (2004–2014)                             | Retrospective Study | 7   | YG ≤40    | 152 | 33.7±5.54 | Male   | Upper | 178 | 72 | 75 | 39 | 32 | 66 | 15 |
|              |         |                                                      |                   |     | YG >40    | 250 | 62.9±10.4 | Male   | Upper | 75 | 53 | 115 | 141 | 35 | 52 | 22 |
| Adachi et al. (28) | Japan     | GC underwent surgery (1981–1990)                      | Retrospective Study | 7   | YG ≤40    | 36  | 20 | 16 | – | – | 16 | 5 | 8 | 7 |
|              |         |                                                      |                   |     | YG >60    | 68  | 43 | 25 | – | – | 25 | 13 | 16 | 14 |
| Bautista et al. (29) | United States | Non-cardia GAC (2000–2010)                    | Retrospective Cohort Study | 8   | YG ≤40    | 46  | 24 | 22 | 1 | 10 | 14 | – | – | – | – |
|              |         |                                                      |                   |     | YG ≥50    | 1,208 | 71.5±3.8 | Male | Upper | 198 | 714 | 494 | 65 | 379 | 426 | – | – | – | – |
| Wang et al. (30) | China   | GC underwent curative gastrectomy (2005–2010)        | Retrospective Study | 8   | YG ≤40    | 342 | 34.4±5.3 | Male   | Upper | 198 | 714 | 494 | 65 | 379 | 426 | – | – | – | – |
|              |         |                                                      |                   |     | YG >40    | 3,588 | 2,448 | 1,140 | 841 741 1,783 | 876 | 927 | 1,522 | 263 |

No., number of patients; pTNM, pathological (p), primary tumor (T), lymph nodes (N) and distant metastases (M); GC, gastric cancer; GAC, gastric adenocarcinoma.
Table 2 Subgroup meta-analysis of clinicopathological characteristics and survival outcomes between the younger group and older group

| Subgroup                        | Included studies | Included patients | $I^2$ (%) | Effect model | OR/WMD | 95% CI      | P       |
|---------------------------------|------------------|-------------------|-----------|--------------|--------|-------------|---------|
| Female                          | 25               | 81,188            | 76        | Random       | 2.09   | 1.81–2.41   | <0.001  |
| Diffuse type                    | 10               | 56,335            | 82        | Random       | 4.29   | 3.15–5.85   | <0.001  |
| pTNM stage IV                   | 16               | 26,202            | 0         | Fixed        | 1.21   | 1.08–1.35   | <0.001  |
| Poorly differentiation          | 19               | 75,349            | 82        | Random       | 3.59   | 2.89–4.47   | <0.001  |
| SRCC                            | 5                | 52,262            | 0         | Fixed        | 4.81   | 4.33–5.33   | <0.001  |
| Therapeutic regimen             |                  |                   |           |              |        |             |         |
| Subtotal gastrectomy            | 9                | 14,427            | 39        | Fixed        | 0.88   | 0.79–0.99   | 0.03    |
| Curative gastrectomy            | 14               | 18,159            | 10        | Fixed        | 0.93   | 0.82–1.06   | 0.30    |
| D1 lymphadenectomy              | 4                | 7,387             | 25        | Fixed        | 0.59   | 0.48–0.73   | <0.001  |
| ≥ D2 lymphadenectomy            | 4                | 7,387             | 27        | Fixed        | 1.77   | 1.44–2.18   | <0.001  |
| Chemotherapy                    | 6                | 8,750             | 43        | Fixed        | 1.79   | 1.49–2.16   | <0.001  |
| Postoperative complications     | 5                | 6,309             | 73        | Random       | 0.44   | 0.24–0.79   | 0.006   |
| Recurrence/metastasis           |                  |                   |           |              |        |             |         |
| Peritoneal recurrence           | 4                | 1,965             | 11        | Fixed        | 1.93   | 1.31–2.84   | 0.001   |
| Lymph node metastasis           | 8                | 3,901             | 0         | Fixed        | 0.83   | 0.69–0.98   | 0.03    |
| Hepatic metastasis              | 9                | 11,126            | 0         | Fixed        | 0.68   | 0.47–0.98   | 0.04    |
| Peritoneal metastasis           | 9                | 11,695            | 63        | Random       | 1.63   | 1.16–2.27   | 0.004   |
| 5-year OS                       | 9                | 59,647            | 60        | Random       | 1.01   | 0.79–1.30   | 0.92    |
| 5-year OS underwent surgery     | 18               | 26,770            | 56        | Random       | 1.35   | 1.16–1.57   | <0.001  |
| Stage I-OS                      | 8                | 6,536             | 11        | Fixed        | 2.38   | 1.56–3.61   | <0.001  |
| Stage II-OS                     | 8                | 3,347             | 46        | Fixed        | 1.28   | 0.98–1.66   | 0.07    |
| Stage III-OS                    | 7                | 5,702             | 27        | Fixed        | 1.36   | 1.14–1.63   | <0.001  |
| Stage IV-OS                     | 7                | 1,483             | 0         | Fixed        | 1.93   | 1.30–2.85   | 0.001   |
| 5-year OS underwent curative surgery | 12              | 19,012            | 60        | Random       | 1.39   | 1.12–1.72   | 0.002   |
| Stage I-OS                      | 4                | 5,261             | 51        | Random       | 1.73   | 0.86–3.49   | 0.13    |
| Stage II-OS                     | 4                | 2,771             | 51        | Random       | 0.95   | 0.60–1.51   | 0.83    |
| Stage III-OS                    | 4                | 4,639             | 0         | Fixed        | 1.29   | 1.05–1.58   | 0.01    |
| Stage IV-OS                     | 3                | 1,016             | 0         | Fixed        | 1.86   | 1.20–2.89   | 0.006   |

pTNM, pathological (p), primary tumor (T), lymph nodes (N) and distant metastases (M); SRCC, signet ring cell carcinoma; OS, overall survival.
were no statistical differences in curative resection rate between the two groups (OR =0.93; 95% CI: 0.82–1.06, P=0.30, I²=10%) (Figure S3).

**Postoperative complications**

A total of 6,309 patients from five studies were enrolled in postoperative complications. The result revealed that the proportion of complications in younger patients was significantly lower compared to the older (OR =0.44, 95% CI: 0.24–0.79, P=0.006), and the heterogeneity between the younger and older group was significant (I²=73%) (Figure S4).

**Survival outcomes**

*Figure 2* presented the meta-analysis of the 5-year overall survival (OS) with total patients, gastrectomy group, and only curative gastrectomy group, respectively. There was no significant difference for total patients based on the nine included studies (OR =1.01, 95% CI: 0.79–1.30, P=0.92, I²=60%). However, the pooled 18 and 12 studies respectively showed that younger adults in gastrectomy group and only curative gastrectomy group were associated with better survival relative to that of the older (OR =1.35, 95% CI: 1.16–1.57, P<0.001, I²=56%; OR =1.39, 95% CI: 1.12–1.72, P=0.002, I²=60%).

Moreover, further survival analyses between younger and older patients were done under the different pTNM tumor stage. Four of the studies provided survival rates for gastrectomy group, and the meta-analysis showed that younger patients at pTNM stage I, stage III, and stage IV were associated with better 5-year OS than older (OR =2.38, 95% CI: 1.56–3.61, P<0.001, I²=11%; OR =1.36, 95% CI: 1.14–1.63, P<0.001, I²=27%; OR =1.93, 95% CI: 1.30–2.85, P=0.001, I²=0%, respectively) (Figure 3). For the only curative gastrectomy group, three of the included studies revealed that younger patients at pTNM stage III and stage IV also had improved survival (OR =1.29, 95% CI: 1.05–1.58, P=0.01, I²=0%; OR =1.86, 95% CI: 1.20–2.89, P=0.006, I²=0%, respectively), but there was no statistical difference in gastric cancer at stage I (OR =1.73, 95% CI: 0.86–3.49, P=0.13, I²=51%) (Figure 4). The short-term (including the 1-, 2-, 3-year) survival rates were presented in Table S2.

Concerning to the metastasis status of gastric cancer, nine of the 25 studies showed that younger group was predominant in peritoneal metastasis (OR =1.63, 95% CI: 1.16–2.27, P=0.004, I²=63%). Some included studies reported the lymph node metastasis and hepatic metastasis of gastric cancer, and our result showed that both lymph node metastasis and hepatic metastasis ratio was lower in younger group compared with those of the older (OR =0.83, 95% CI: 0.69–0.98, P=0.03, I²=0%; OR =0.68, 95% CI: 0.47–0.98, P=0.04, I²=0%). In addition, 4 related studies indicated that the incidence of peritoneal recurrence was significantly higher in younger group (OR =1.93, 95% CI: 1.31–2.84, P=0.001, I²=11%) (Figure S5 and Table S3).

**Discussion**

The review and meta-analysis involved 24 retrospective comparative trails and one prospective study with 81,188 patients with gastric cancer. Our findings demonstrated that the younger group after gastrectomy or only curative gastrectomy was correlated with a better OS, but there was no significant difference for total patients between the two groups. To our best knowledge, this analysis was the most extensive evaluation to compare the clinicopathological feature and prognosis between the younger and older group.

Several findings regarding the clinicopathological characteristics in the meta-analysis were in agreement with previous researches, including a higher proportion of female, poorly differentiation, signet ring cell carcinoma, diffuse histology, and pTNM tumor stage IV in younger adults (8-21). Our survey revealed that younger patients had a higher proportion of females, while male predominance was mostly seen in the older group. Although the reasons for female predominance in younger patients were not clear, some potential explanations had been identified. Several studies considered hormonal factors, such as estrogens and higher percentages of estrogen receptor-positive cells might be associated with the predominance of younger females (36,37). Compared to older patients, younger patients with gastric cancer had been believed to be related to genetic changes rather than environmental factors (38). Thereby more frequent exposure to environmental carcinogens, such as cigarettes, might lead to the dominance among older male patients (39). Concerning to histological type, our analysis revealed that poorly differentiation, diffuse-type, and signet ring cell carcinoma were predominant in the younger group. In comparison, more patients in the older group were diagnosed as intestinal type and mucous adenocarcinoma. The primary reason may be germline mutations, specifically in the CDH1 gene, as reported in...
Figure 2 The 5-year overall survival for gastric cancer between younger and older group. (A) The 5-year overall survival of total patients; (B) the 5-year overall survival of patients underwent gastrectomy; (C) the 5-year overall survival of patients underwent curative gastrectomy.
Figure 3 The 5-year overall survival of gastric cancer underwent gastrectomy between younger and older group. (A) Meta-analysis of patients at pTNM stage I; (B) meta-analysis of patients at pTNM stage II; (C) meta-analysis of patients at pTNM stage III; (D) meta-analysis of patients at pTNM stage IV.
some researches (26,40,41). While the included studies rarely capture the duration of symptoms before initial diagnosis, other researches have reported delayed diagnosis, and hereditary factors may be closely correlated with advanced gastric cancer (42,43).

Surgery, especially curative resection, was an important approach for patients with gastric cancer (44). There were higher proportions of chemotherapy and ≥D2 lymphadenectomy in the younger group compared with the older. However, the percentages of total gastrectomy and curative resection revealed no statistical differences between younger and older groups, while subtotal gastrectomy was frequently performed in older patients. These results may be due to the significant comorbidities and impairment of functional status in older patients (45-47). Moreover, a previous study demonstrated that the ratio of older patients who had other synchronous or previous malignancies at initial diagnosis was up to 21% based on Munich Cancer Registry data (48). In our review, postoperative complications were more prevalent in the

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**Figure 4** The 5-year overall survival of gastric cancer underwent curative gastrectomy between younger and older group. (A) Meta-analysis of patients at pTNM stage I; (B) meta-analysis of patients at pTNM stage II; (C) meta-analysis of patients at pTNM stage III; (D) meta-analysis of patients at pTNM stage IV.
older group, which also reflected a worse tolerance for surgery or chemotherapy. Several studies investigated that the incidence of postoperative complications was closely correlated with poor prognosis (49,50), thus providing a survival advantage for the younger group.

In this analysis, a tendency of peritoneal metastasis in the younger group may reflect the genetic susceptibility, such as CDH1 and RhoA, that could lead to more aggressive biological behaviors (40,51). Moreover, the infiltration of poorly differentiated gastric cancer was more pronounced in the vertical direction, thus conferring lymph node involvement and peritoneal dissemination. Metastasis was the leading cause of recurrence, and it had been thought that peritoneal metastasis was the most common form of repetition in gastric carcinoma (15). Our finding indicated a higher incidence of peritoneal recurrence in younger patients, which was similar to the other conclusion (12).

Younger gastric cancer patients as a group revealed similar long-term OS compared to older, and this finding was consistent with previous studies (5,10,11,20). In the subgroups of gastrectomy and only curative gastrectomy, both the short-term (including the 1-, 2-, 3-year) and long-term (including the 5-year) OS for older group was more miserable than those of the younger group, possibly due to a more significant percentage of comorbidities and complications. When the 5-year OS under different pTNM stages was evaluated, the results differed substantially between the younger and older group. A trend towards better long-term survival in the younger group may reflect a higher tolerance for the patients given a younger age and fewer comorbidities. Moreover, the shorter life expectancy of the older group compared to the younger may also be responsible.

There were several limitations in the analysis because of the characteristics of the included studies identified. Firstly, only one of the trials we identified was a prospective study. Secondly, most of the included studies were from Eastern Asia, which might not have a great representative and guiding value across the globe, especially in Western countries. Thereby, more related researches were expected to evaluate in gastric cancer patients at a younger age. Thirdly, there were inevitable heterogeneities, such as female ratio, diffuse type, as well as several survival variables in the analysis. The contribution of each included study to the pooled estimate was evaluated in the sensitivity analyses, and the result showed that sources of these heterogeneities were mainly from the selection bias. Furthermore, the lack of available patient data did not allow our analysis to assess disease-specific survival and disease-free survival. Despite these limitations, the study to our knowledge was the most extensive analysis evaluating the clinicopathological characteristics and survival outcomes in the younger and older patients, which may overcome the limitation of small sample size and single-institution targeted the field. Besides, all of the clinical studies involved in the meta-analysis had a high quality and met our inclusion criteria, thus might provide more valuable resources for the clinicians in patients’ management and decision-making.

Conclusions

In conclusion, younger patients with gastric cancer were more often diagnosed as poorly differentiation and later pTNM tumor stage. However, younger cancer patients following gastrectomy had a better OS rate than patients in older group. Future large-scale analyses are expected to confirm our findings.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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### Table S1: Clinicopathological characteristics of the included 25 studies

| Authors               | Group    | No. | Tumor size ± SD (cm) | Pain | Bleeding | Cardiopulmonary disease | Differentiation | SRCC | Mucinous | Lauren type | Bormann classification |
|-----------------------|----------|-----|----------------------|------|----------|-------------------------|----------------|------|----------|-------------|------------------------|
| Song et al. (4)       | OG       | 358 | ≤6 n=239; >6 n=119   | –    | –        | –                       | 83             | 275  | –        | –           | –                      |
| Cormedi et al. (9)    | OG       | 223 | –                    | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Tavares et al. (8)    | OG       | 360 | 160 ±100             | –    | –        | –                       | 56             | 89   | –        | –           | –                      |
| Guan et al. (9)       | OG       | 46,521 | 4.00±1.47         | –    | –        | –                       | 2493           | 22,616 5756 | 990 | 37,799 | 7,021| –          | –                     |
| Isobe et al. (10)     | OG       | 3,649 | –                 | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Kim et al. (11)       | OG       | 194 | 5.16±3.45           | –    | –        | –                       | –              | –    | 6 10     | –           | –                     |
| Kunisaki et al. (12)  | OG       | 1,096 | 29                | –    | –        | –                       | 123            | 587  | –        | –           | –                      |
| Liu et al. (13)       | OG       | 198 | 0                  | –    | –        | –                       | 7              | 164   | –        | –           | –                      |
| Okamoto et al. (14)   | OG       | 34  | –                   | –    | –        | –                       | 22             | 2 0   | –        | –           | 0/20 0 12 4          |
| Takatsu et al. (15)   | OG       | 132 | –                   | –    | –        | –                       | 51             | 1 5   | –        | –           | 3/85 25 34 14        |
| Tekesin et al. (16)   | OG       | 92  | 22 ±0.6             | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Wang et al. (17)      | OG       | 774 | 191 ±52             | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Wang et al. (17)      | OG       | 21  | <5 n=13; ≥5 n=8     | –    | –        | –                       | 4              | 10 ±4 1 | –        | –           | 1 6 12 2             |
| Hsieh et al. (18)     | OG       | 115 | 4.80±3.50           | –    | –        | –                       | 17             | 98   | –        | –           | –                      |
| Ma et al. (19)        | OG       | 1,099 | 4.50±3.00          | –    | –        | –                       | 453            | 556  | –        | –           | –                      |
| Mitsuomi et al. (20)  | OG       | 128 | 48 ±6               | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Kulig et al. (21)     | OG       | 214 | 90 ±12              | –    | –        | –                       | –              | 42   | 80 ±18  | –           | –                      |
| Bani-Hani et al. (22) | OG       | 3,217 | –                 | 1831| 186 293 | –                       | –              | 1,106 | 623 207 | –           | –                      |
| Kim et al. (23)       | OG       | 175 | –                   | –    | –        | –                       | 42             | 133   | –        | –           | –                      |
| Lai et al. (24)       | OG       | 1,124 | –                | –    | –        | –                       | 608            | 516  | –        | –           | –                      |
| Zhou et al. (27)      | OG       | 883 | ≤4 n=586; >4 n=288  | –    | –        | –                       | 135            | 711   | –        | –           | 10 114 297 75        |
| Maehara et al. (25)   | OG       | 6,071 | ≤4 n=354; >4 n=2,488| –    | –        | –                       | 2,661          | 3,232 | –        | –           | 665 812 2,039 405    |
| Silva et al. (26)     | OG       | 174 | 7.10±4.20           | –    | –        | –                       | 39             | 135   | –        | –           | –                      |
| Zhou et al. (24)      | OG       | 453 | ≤5 n=179; >5 n=259  | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Zhou et al. (27)      | OG       | 152 | 73 ±19              | –    | –        | –                       | –              | –    | –        | –           | –                      |
| Adachi et al. (28)    | OG       | 250 | 98 ±11              | –    | –        | –                       | –              | 156  | 73 21   | –           | –                      |
| Bautista et al. (29)  | OG       | 36  | 6 ±23               | –    | –        | –                       | 0              | 33   | –        | –           | –                      |
| Wang et al. (30)      | OG       | 3,588 | –                 | –    | –        | –                       | –              | –    | –        | –           | –                      |
**Figure S1** Meta-analysis of female ratio between younger and older group.

| Study or Subgroup | Younger group | Older group | Odds Ratio | M-H Random, 95% CI |
|-------------------|---------------|-------------|------------|--------------------|
|                   | Events | Total | Events | Total | Weight | M-H Random, 95% CI |
| Adachi and Ogawa et al 1994 | 16 | 36 | 25 | 68 | 2.1% | 1.38 [0.61, 3.13] |
| Esmi 2005 | 10 | 17 | 55 | 159 | 1.5% | 2.70 [0.97, 7.49] |
| Baudista and Jiang et al 2014 | 22 | 46 | 494 | 1206 | 3.1% | 1.32 [0.73, 2.39] |
| Cormedi and Katayama et al 2018 | 37 | 71 | 88 | 223 | 3.4% | 1.67 [0.99, 2.88] |
| Guan and Yuan et al 2019 | 641 | 1369 | 18417 | 46521 | 6.3% | 1.34 [1.21, 1.50] |
| Hsieh and Wang et al 2012 | 69 | 115 | 373 | 1009 | 4.4% | 2.56 [1.72, 3.79] |
| Isobe and Hashimoto et al 2013 | 90 | 169 | 1131 | 3649 | 5.0% | 2.54 [1.86, 3.46] |
| Kim and Boo et al 2008 | 75 | 175 | 359 | 1124 | 4.9% | 1.80 [1.16, 2.21] |
| Kim and Joo et al 2005 | 74 | 137 | 63 | 194 | 4.0% | 2.44 [1.56, 3.83] |
| Kulić and Popiel et al 2008 | 95 | 214 | 940 | 3217 | 5.2% | 1.93 [1.46, 2.56] |
| Kunisaki and Akayama et al 2006 | 67 | 131 | 260 | 918 | 4.5% | 2.65 [1.83, 3.84] |
| Lai and Kim et al 2008 | 407 | 883 | 1876 | 6071 | 6.1% | 1.91 [1.66, 2.21] |
| Liu and Feng et al 2016 | 83 | 198 | 201 | 1096 | 4.9% | 3.21 [2.33, 4.43] |
| Ma and Ren et al 2016 | 49 | 125 | 411 | 1752 | 4.5% | 2.10 [1.44, 3.06] |
| Maehara and Emi et al 1996 | 95 | 174 | 109 | 356 | 4.5% | 2.16 [1.49, 3.14] |
| Mitsudomi and Matsusaka et al 1999 | 62 | 128 | 412 | 1275 | 4.8% | 1.97 [1.36, 2.84] |
| Okamoto and Makino et al 1988 | 24 | 34 | 35 | 132 | 2.0% | 6.65 [2.89, 15.30] |
| Silva and Begrami et al 2008 | 24 | 62 | 165 | 453 | 3.4% | 1.10 [0.84, 1.49] |
| Song and Li et al 2017 | 53 | 112 | 84 | 358 | 4.0% | 2.93 [1.88, 4.57] |
| Takatsu and Hiki et al 2016 | 64 | 136 | 411 | 1435 | 4.6% | 2.21 [1.55, 3.16] |
| Tavares and Gandra et al 2013 | 11 | 23 | 153 | 360 | 2.0% | 1.24 [0.53, 2.69] |
| Tekesin and Gunes et al 2019 | 39 | 92 | 221 | 774 | 4.0% | 1.84 [1.18, 2.88] |
| Wang and Hsieh et al 1996 | 12 | 21 | 14 | 36 | 1.4% | 2.10 [0.70, 6.25] |
| Wang and Xu et al 2016 | 144 | 342 | 1140 | 3588 | 5.6% | 1.56 [1.25, 1.98] |
| Zhou and Shi et al 2015 | 99 | 152 | 72 | 250 | 4.1% | 4.62 [3.00, 7.11] |

Total (95% CI): 4962 / 76226 / 100.0% / 2.09 [1.81, 2.41]
Figure S2 The proportion of clinicopathologic feature between younger and older group. (A) Meta-analysis of diffuse type; (B) meta-analysis of pTNM stage IV; (C) meta-analysis of poorly differentiation; (D) meta-analysis of signet ring cell carcinoma.
Figure S3 The proportion of therapeutic regimen between younger and older group. (A) Meta-analysis of subtotal gastrectomy; (B) meta-analysis of D1 lymphadenectomy; (C) meta-analysis of chemotherapy; (D) meta-analysis of curative resection.
Figure S4 Meta-analysis of the proportion of postoperative complications between younger and older group.
Table S2 Subgroup meta-analysis of overall survival comparison between the younger group and older group

| Subgroup                                      | Included studies | Included patients | I² (%) | Effect model | OR/WMD   | 95% CI       | P        |
|-----------------------------------------------|------------------|-------------------|--------|--------------|----------|--------------|----------|
| OS                                            |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 8                | 59,132            | 81     | Random       | 1.08     | 0.80–1.45   | 0.63     |
| 2-year OS                                     | 8                | 59,132            | 78     | Random       | 1.04     | 0.79–1.36   | 0.79     |
| 3-year OS                                     | 8                | 59,132            | 74     | Random       | 1.01     | 0.78–1.32   | 0.93     |
| 5-year OS                                     | 9                | 59,647            | 60     | Random       | 1.01     | 0.79–1.30   | 0.92     |
| OS underwent gastrectomy                      |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 15               | 18,442            | 0      | Fixed        | 1.20     | 1.04–1.39   | 0.01     |
| 2-year OS                                     | 15               | 18,442            | 56     | Random       | 1.31     | 1.08–1.58   | 0.005    |
| 3-year OS                                     | 15               | 18,442            | 1      | Fixed        | 1.33     | 1.19–1.48   | <0.001   |
| 5-year OS                                     | 18               | 26,770            | 56     | Random       | 1.35     | 1.16–1.57   | <0.001   |
| Stage I-OS underwent gastrectomy              |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 5                | 5,437             | 0      | Fixed        | 5.18     | 1.03–26.03  | 0.05     |
| 2-year OS                                     | 5                | 5,437             | 0      | Fixed        | 2.29     | 1.11–4.71   | 0.02     |
| 3-year OS                                     | 5                | 5,437             | 0      | Fixed        | 3.32     | 1.72–6.40   | <0.001   |
| 5-year OS                                     | 8                | 6,536             | 11     | Fixed        | 2.38     | 1.56–3.61   | <0.001   |
| Stage II-OS underwent gastrectomy             |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 5                | 2,735             | 0      | Fixed        | 1.54     | 0.72–3.33   | 0.27     |
| 2-year OS                                     | 5                | 2,735             | 0      | Fixed        | 1.25     | 0.80–1.94   | 0.33     |
| 3-year OS                                     | 5                | 2,735             | 45     | Fixed        | 1.47     | 1.01–2.14   | 0.04     |
| 5-year OS                                     | 8                | 3,347             | 46     | Fixed        | 1.28     | 0.98–1.66   | 0.07     |
| Stage III-OS underwent gastrectomy            |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 5                | 4,499             | 61     | Random       | 1.41     | 0.81–2.45   | 0.22     |
| 2-year OS                                     | 5                | 4,499             | 55     | Random       | 1.53     | 1.07–2.20   | 0.02     |
| 3-year OS                                     | 5                | 4,499             | 60     | Random       | 1.62     | 1.14–2.31   | 0.007    |
| 5-year OS                                     | 7                | 5,702             | 27     | Fixed        | 1.36     | 1.14–1.63   | <0.001   |
| Stage IV-OS underwent gastrectomy             |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 5                | 1,341             | 74     | Random       | 1.18     | 0.54–2.58   | 0.68     |
| 2-year OS                                     | 5                | 1,341             | 83     | Random       | 3.46     | 1.26–9.56   | 0.02     |
| 3-year OS                                     | 5                | 1,341             | 41     | Fixed        | 1.77     | 1.23–2.54   | 0.002    |
| 5-year OS                                     | 7                | 1,483             | 0      | Fixed        | 1.93     | 1.30–2.85   | 0.001    |
| OS underwent curative surgery                 |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 11               | 12,660            | 0      | Fixed        | 1.35     | 1.05–1.72   | 0.02     |
| 2-year OS                                     | 11               | 12,660            | 33     | Fixed        | 1.22     | 1.03–1.45   | 0.02     |
| 3-year OS                                     | 11               | 12,660            | 0      | Fixed        | 1.36     | 1.17–1.58   | <0.001   |
| 5-year OS                                     | 12               | 19,012            | 60     | Random       | 1.39     | 1.12–1.72   | 0.002    |
| Stage I-OS underwent curative surgery         |                  |                   |        |              |          |              |          |
| 5-year OS                                     | 4                | 5,261             | 51     | Random       | 1.73     | 0.86–3.49   | 0.13     |
| Stage II-OS underwent curative surgery        |                  |                   |        |              |          |              |          |
| 5-year OS                                     | 4                | 2,771             | 51     | Random       | 1.07     | 0.80–1.43   | 0.67     |
| Stage III-OS underwent curative surgery       |                  |                   |        |              |          |              |          |
| 5-year OS                                     | 4                | 4,639             | 0      | Fixed        | 1.29     | 1.05–1.58   | 0.01     |
| Stage IV-OS underwent curative surgery        |                  |                   |        |              |          |              |          |
| 5-year OS                                     | 3                | 1,016             | 0      | Fixed        | 1.86     | 1.20–2.89   | 0.006    |
| OS underwent Non-curative surgery             |                  |                   |        |              |          |              |          |
| 1-year OS                                     | 3                | 268               | 70     | Random       | 1.31     | 0.40–4.29   | 0.66     |
| 2-year OS                                     | 3                | 268               | 38     | Fixed        | 0.92     | 0.49–1.71   | 0.87     |
| 3-year OS                                     | 3                | 268               | 0      | Fixed        | 1.37     | 0.72–2.61   | 0.34     |
| 5-year OS                                     | 3                | 268               | 0      | Fixed        | 1.14     | 0.56–2.36   | 0.72     |

stage, pTNM stage. OS, overall survival.
Figure S5 The proportion of metastasis and recurrence between younger and older group. (A) Meta-analysis of peritoneal recurrence; (B) meta-analysis of peritoneal metastasis; (C) meta-analysis of lymph node metastasis; (D) meta-analysis of hepatic metastasis.
Table S3 Therapeutic regimens and survival outcomes of the included studies

| Authors          | Group | No. | Type of gastrectomy | Resection margin | Lymphadenectomy | Chemotherapy | Complication | Peritoneal recurrence | Metastasis |
|------------------|-------|-----|---------------------|------------------|-----------------|--------------|--------------|----------------------|------------|
| Song et al. (4)  | YG    | 112 | – –                 | 85 27            | – –             | – –          | – –          | – –                  | – – – –    |
|                  | OG    | 358 | – –                 | 260 98           | – –             | – –          | – –          | – –                  | – – – –    |
| Cornedi et al. (5)| YG   | 71  | – –                 | – –             | – –             | 21            | – –          | – –                  | – – – –    |
|                  | OG    | 223 | – –                 | – –             | – –             | 59            | – –          | – –                  | – – – –    |
| Tavares et al. (8)| YG   | 23  | 4 19                | – –             | – –             | 9             | – –          | 3                    | 1 – – –    |
|                  | OG    | 360 | 133 227            | – –             | – –             | 86            | – –          | 10                   | – – 21 –   |
| Guan et al. (9)  | YG    | 1,349 | – –                 | – –             | – –             | – –          | – –          | – –                  | – – – –    |
|                  | OG    | 46,521 | – –                 | – –             | – –             | – –          | – –          | – –                  | – – – –    |
| Isobe et al. (10) | YG    | 169 | – 52                | 112 3 30 119     | 69              | – –          | – –          | 4                    | 33         |
|                  | OG    | 3,649 | – 936               | 2,728 217 988 2,205 | 1,180          | – –          | – –          | – – 203               | 414        |
| Kim et al. (11)  | YG    | 137 | 78 47               | 101             | – –             | – –          | – –          | 70                   | 5 21       |
|                  | OG    | 194 | 122 52              | 157             | – –             | – –          | – –          | 106                  | 6 18       |
| Kuniyoshi et al. (12)| YG | 131 | 93 25               | 121             | – –             | 24 107       | – –          | 18                   | 48 34 2 6 |
|                  | OG    | 918 | 644 274            | 827             | – –             | 280 638      | – –          | 61                   | 397 332 22 44 |
| Liu et al. (13)  | YG    | –   | – –                 | – –             | – –             | – –          | – –          | – –                  | – – – –    |
|                  | OG    | –   | – –                 | – –             | – –             | – –          | – –          | – –                  | – – – –    |
| Okamoto et al. (14) | YG  | 34  | – –                 | 15 10            | – –             | – –          | – –          | 19                   | 2 13       |
|                  | OG    | 132 | – –                 | 73 23            | – –             | – –          | – –          | 64                   | 10 20      |
| Takatsuki et al. (15) | YG  | 126 | – 32                | 114 22           | – –             | 14 6         | – –          | 33/1,14              | – – – –    |
|                  | OG    | 1,435 | – 445               | 1,241 194       | – –             | 276 58       | – –          | 33/1,241             | – – – –    |
| Tokesin et al. (16) | YG  | 92  | 17 32               | – –             | – –             | – –          | – –          | 29                   | – 26       |
|                  | OG    | 774 | 195 260            | – –             | – –             | – –          | – –          | 254                  | – 230      |
| Wang et al. (17) | YG    | 21  | – –                 | 19               | – –             | – –          | 4            | – –                  | – 20 – 76 |
|                  | OG    | 1,263 | – –                | 490             | – –             | 9            | – –          | 25                   | – – – –    |
| Hsieh et al. (18) | YG    | 115 | 84 31               | 101 14           | – –             | 82            | – –          | 12                   | – – – –    |
|                  | OG    | 1,009 | 753                | 256 893 116     | – –             | 590           | – –          | 25                   | – – – –    |
| Ma et al. (19)   | YG    | 125 | – –                 | – –             | – –             | 96            | – –          | –                    | – 43 – –   |
|                  | OG    | 1,752 | – –               | 1,023           | – –             | – –          | – –          | 451                  | – – – –    |
| Mitsudomi et al. (20) | YG  | 128 | 13 29               | 103             | – –             | 9             | – –          | –                    | – – – –    |
|                  | OG    | 1,275 | 90 236           | 1,076           | – –             | 15            | – –          | –                    | – – – –    |
| Kuroi et al. (21) | YG    | 214 | 89 63               | 78 74           | – –             | 113           | – –          | 65                   | – – – –    |
|                  | OG    | 3,217 | 1,195            | 898 1,146 947   | 641 1,452      | 1,058        | – –          | – –                  | – – – –    |
| Bani-Hani et al. (22) | YG  | 17  | – –                 | 7               | – –             | – –          | – –          | –                    | – – – –    |
|                  | OG    | 159 | – –                 | 66              | – –             | – –          | – –          | –                    | – – – –    |
| Kim et al. (23)  | YG    | 175 | – –                 | 144 31          | – –             | – –          | 86           | – –                  | – – – –    |
|                  | OG    | 1,124 | – –               | 888 236        | – –             | – –          | 566          | – –                  | – – – –    |
| Lai et al. (24)  | YG    | 883 | 612 262            | – –             | – –             | – –          | – –          | – –                  | – – – –    |
|                  | OG    | 6,071 | 4,491            | 1,519          | – –             | – –          | – –          | – –                  | – – – –    |
| Maehara et al. (25) | YG  | 174 | 112 62              | 125             | – –             | 32 141       | – –          | 15                   | 95 15 2 23 |
|                  | OG    | 356 | 212 139            | 255             | – –             | 119 237      | – –          | 25                   | 207 81 16 23 |
| Silva et al. (26) | YG    | –  | – –                 | – –             | – –             | – –          | 38           | – –                  | – – – –    |
|                  | OG    | –  | – –                 | – –             | – –             | – –          | 342          | – –                  | – – – –    |
| Adachi et al. (28) | YG^3  | 36  | – –                 | – –             | – –             | 7            | – –          | 17                   | – 1/7 4/7 |
|                  | OG^1  | 68  | – –                 | – –             | – –             | 25           | – –          | 33                   | – 3/24 7/24 |
| Bautista et al. (29) | YG  | 46  | – –                 | – –             | – –             | 31           | – –          | – –                  | – – – –    |
|                  | OG    | 1,208 | – –               | 475            | – –             | – –          | – –          | – –                  | – – – –    |
| Wang et al. (30)  | YG    | 342 | – –                 | 327 15          | – –             | 267          | – –          | 16                   | 13         |
|                  | OG    | 3,588 | – –               | 3,406 182       | – –             | 2,856        | – –          | 165                  | 173        |

No., number of patients; YG, younger group; OG, older group; R, resection margin.