Addition of Taxanes to Platinum and Fluoropyrimidines in Adjuvant Setting Did Not Improve Survival in Patients with Gastric Cancer after Curative Gastrectomy

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Research article

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Abstract

Background

To evaluate whether the addition of taxane to platinum and fluoropyrimidines in adjuvant chemotherapy would result in longer survival than platinum plus fluoropyrimidines in patients who underwent curative gastrectomy.

Methods

This study retrospectively analyzed survival for patients with stage Ⅱ-Ⅲ gastric adenocarcinoma who received curative gastrectomy and adjuvant chemotherapy with platinum plus fluoropyrimidines (PF group) or taxanes and platinum plus fluoropyrimidines (TPF group). Survival curves were estimated using the Kaplan-Meier method, and the differences were compared using the log-rank test.

Results

Baseline characteristics were balanced between the PF group and TPF group. The median disease-free survival (DFS) was 14.9 months (*95% CI*: 11.0-18.8) in the PF group and 13.8 months (*95% CI*: 9.3-18.3) in the TPF group (*HR*=0.90, *95% CI*: 0.63-1.29, *log-rank test*, *P*=0.560). The median overall survival (OS) was 30.0 months for patients in the PF group (*95% CI*: 24.5-35.5) and 25.6 months (*95% CI*: 22.3-28.9) for those in the TPF group (*HR*=0.93, *95% CI*: 0.64-1.35, *log-rank test*, *P*=0.705).

Conclusion

For stage Ⅱ-Ⅲ gastric adenocarcinoma, the adjuvant triple combination of TPF regimen after curative gastrectomy did not demonstrate survival benefit compared to the PF regimen.

Background

It was estimated that there are more than 1 million incident gastric cancer cases worldwide every year, of which 44% were diagnosed in China [1]. For resectable cases, surgery is the only curative approach, either alone or in combination with perioperative treatment. Radical gastrectomy with D2 lymphadenectomy followed by adjuvant chemotherapy is now considered as standard of care for most gastric cancers in Asian countries [2]. Monotherapy or doublet regimens were frequently used in adjuvant settings. According to results of randomized clinical trials, oxalipatin plus capecitabine or S1 monotherapy were recommended adjuvant regimens [3, 4]. In fact, in actual clinical practice, varied doublet combinations of platinum (oxalipatin, cisplatin, or lobaplatin) with fluoropyrimidines (5-fluorouracil, capecitabine or S1) were all universally acceptable adjuvant regimens. Taxanes, which mainly consist of docetaxel or paclitaxel, are effective in gastric cancer treatment and were also tested in adjuvant settings. In the Stomach Cancer Adjuvant Multi-Institutional Group Trial (SAMIT), sequential paclitaxel followed by oral fluoropyrimidines as adjuvant chemotherapy for T4a/b gastric cancer did not improve disease-free survival (DFS) compared to oral fluoropyrimidines [5]. However, recently, docetaxel plus S1 was

demonstrated to be superior to S1 monotherapy in stage □ gastric cancer treatment [6]. Triple combination chemotherapeutic regimens added with taxanes are usually used in perioperative or palliative settings for patients with good performance status [7, 8]. Whether the addition of docetaxel or paclitaxel to the traditional combination of platinum and fluoropyrimidines as adjuvant regimen could improve survival for gastric cancer had not been explored in clinical trials. This retrospective study used real-world data from clinical practice and attempted to investigate the value of the triple combination regimen with taxanes in the adjuvant chemotherapy of patients with resectable stage □-□ gastric cancer.

Materials And Methods

Patients

This retrospective study consisted of 156 patients diagnosed with gastric adenocarcinoma in the First Affiliated Hospital of Anhui Medical University, Hefei, Anhui Province, China, from 2008 to 2016. All patients included in the study met the following criteria: underwent curative gastrectomy followed by adjuvant chemotherapy; with detailed postoperative pathological report and with stage □ or □ disease according to the American Joint Committee on Cancer (AJCC) seventh staging system; with definite medical records of recurrence or metastasis after surgical resection and available details on systemic adjuvant chemotherapy; received at least one cycle of systemic adjuvant chemotherapy; adjuvant chemotherapeutic regimens should be as doublet combination of platinum and fluoropyrimidines or triple combination of taxanes, platinum, and fluoropyrimidines. For platinum drugs, it could be cisplatin, oxaliplatin, or lobaplatin; for fluoropyrimidine compounds, intravenous 5-fluorouracil injection, oral capecitabine tablets, or tegafur-gimeracil-oteracil potassium capsules were all acceptable; taxanes could either be docetaxel or paclitaxel. In consideration of tolerance to toxicity, drug accessibility, etc., patients whose adjuvant chemotherapeutic drugs were switched from one platinum drug to another, or one fluoropyrimidine compound to another, or docetaxel to paclitaxel (vice versa) in different cycles were considered eligible. Patients who met any of following criteria were excluded from the study: did not receive curative surgery; diagnosed as having a very early phase of disease (stage □); with no adjuvant chemotherapy apart from the abovementioned regimens; with missing information on surgery, pathology, adjuvant treatment, or recurrence and metastasis.

Data collection and follow-up

We retrieved the medical records of the patients from the Hospital Information System (HIS), and reviewed all related medical files. The following variables were collected: demographic variables including age and sex as well as pathological variables including tumor location, subtype, grade, tumor infiltration (T category), regional lymph node involvement (N category), vascular or perineuronal invasion by tumors in pathological specimens, and perigastric tumor deposits. Treatment information, including laparotomic approaches, scope of gastrectomy, type of lymphadenectomy, adjuvant chemotherapeutic drugs, date of the first and last dose of chemotherapeutic drug, and cycles of adjuvant chemotherapy, was obtained. Staging groups were derived from the T and N categories according to the AJCC seventh

staging system. The time to chemotherapy after surgery was defined as interval days from primary surgery to the first dose of adjuvant chemotherapy. The duration of adjuvant chemotherapy was defined as interval days from the first to the last dose of chemotherapeutic drug. Recurrence and metastasis were defined as tumor recurrence in situ (anastomotic stoma or gastric remnant) or metastasis to distant organs, lymph node(s), or intraperitoneal implantation after gastrectomy, with evidence of either imaging, cytology, or histopathology. Survival status was obtained from death records in the HIS or telephone follow-up on the patients or their relatives.

Statistical analysis

DFS was defined as interval months between gastrectomy and first evidence of recurrence and metastasis. Overall survival (OS) was defined as interval months between gastrectomy and death date or last follow-up date. For categorical variables, the Chi-square test was used to examine the differences between the two groups; for numerical variables and nonparametric independent samples the Mann-Whitney U test was used. Survival curves were calculated using the Kaplan-Meier method, and differences were compared using the log-rank test. Hazard ratios (HRs) with 95% confidence intervals (CIs) and two-sided *P* values were reported. HRs in subgroups according to baseline characteristics and two-tailed 95% CIs were calculated using the Cox proportional hazards model. All statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Two-sided $P < 0.05$ was considered to be statistically significant. GraphPad Prism 5.01 software (GraphPad Software Inc., San Diego, CA, USA) was used to draw survival curves and forest maps of the subgroup analysis.

Results

Baseline characteristics of the patients

Of 156 eligible patients, 112 patients received systemic adjuvant chemotherapy with platinum plus fluoropyrimidines (PF group), and 44 patients received chemotherapy with a triple combination of taxanes, platinum, and fluoropyrimidines (TPF group). The characteristics between the two groups were compared and results are shown in Table 1. The demographic characteristics, pathological factors, and surgical details of the patients were balanced between the PF group and TPF group.

Details of adjuvant chemotherapy in the two groups

The details of adjuvant chemotherapy are shown in Table 2. With regard to chemotherapeutic drugs, in both groups, approximately 60% of patients were treated with intravenous 5-fluorouracil in adjuvant settings (55.4% in the PF group and 68.2% in the TPF group, *χ2 test*, $P=0.143$); the frequencies of capecitabine and S1 use were also similar, at 29.5% and 23.2% for capecitabine and S1 in the PF group compared to 25.0% and 25.0%, respectively, in the TPF group ($P > 0.05$). More patients in the TPF group were treated with cisplatin than those in the PF group (56.8% vs. 2.7%, $P=0.000$); accordingly, more patients in the PF group were treated with oxaliplatin than those in the TPF group (93.8% vs. 56.8%, $P=0.000$). The proportions of lobaplatin use were comparable between the two groups (7.1% in the PF

group vs. 9.1% in the TPF group, *P* > 0.05). In the TPF group, 50% of patients (22) were treated with docetaxel and 50% were treated with paclitaxel. The median time to chemotherapy after surgery was 37 [*IQR*: 30, 44] days in the PF group and 38 [*IQR*: 32, 45] days in the TPF group (nonparametric test, *P* > 0.05). There was also no difference between the durations of adjuvant chemotherapy in the two groups (median time 127 [*IQR*: 67, 157] days in the PF group vs. 134 [*IQR*: 82, 174] days in the TPF group, *P*=0.265). The accomplished cycles of adjuvant chemotherapy by patients in the two groups were the same.

Disease-free survival

The median DFS was 14.9 months (*95% CI*: 11.0-18.8) in the PF group and 13.8 months (*95% CI*: 9.3-18.3) in the TPF group (*HR*=0.90, *95% CI*: 0.63-1.29, *log-rank test*, *P*=0.560). Survival curves for DFS are shown in Figure 1a. Figure 2 shows a plot of Cox-adjusted DFS *HRs* (with *95% CIs*) for the subgroups with respect to baseline characteristics. There were no differences in the effect of the TPF regimen on DFS relative to the PF regimen across all subgroups according to baseline characteristics.

Overall survival

As shown in Figure 1b, the median OS was 30.0 months for patients in the PF group (*95% CI*: 24.5-35.5) and 25.6 months (*95% CI*: 22.3-28.9) in the TPF group (*HR*=0.93, *95% CI*: 0.64-1.35, *log-rank test*, *P*=0.705). Figure 3 shows that the effect of adjuvant PF regimen on survival relative to TPF regimen was different according to the Borrmann subtype; the PF regimen in patients with Borrmann □/□ cancers resulted in marginally significantly better survival than the TPF regimen (*HR*=1.93, *95% CI*: 1.03-3.62, *P*=0.041). The adjuvant TPF regimen did not show any survival benefit in comparison to the PF regimen in any gastric cancer subgroups.

Discussion

In Asian countries, the survival for stage □-□ gastric cancer patients was improved by D2 gastrectomy followed by adjuvant capecitabine plus oxaliplatin or adjuvant S-1as demonstrated in the CLASSIC trial and ACTS-GC trial [3, 4]. Adjuvant fluoropyrimidine monotherapy or in combination with platinum was also considered as standard of care for resectable gastric cancer. Intensive chemotherapeutic regimens with a triple-drug combination were seldom tested in adjuvant settings. In the present retrospective study, the addition of docetaxel or paclitaxel to the conventional combination of platinum and fluoropyrimidines in adjuvant chemotherapy for patients after curative gastrectomy did not demonstrate any benefit either in DFS or in overall survival.

The addition of docetaxel or paclitaxel in chemotherapy regimens was shown to be effective in advanced gastric cancer [9-11]. For resectable gastric cancer, the results of the SAMIT study showed that sequential paclitaxel followed by fluoropyrimidines did not improve DFS compared to tegafur and uracil (UFT) or S-1 monotherapy [5]. However, the interim analysis of JACCRO GC-07, a randomized controlled trial, demonstrated the superiority of S-1 plus docetaxel to S-1 for 3-year relapse-free survival (66% vs. 50%)

with only few safety concerns in patients with stage III gastric cancer [6]. Intensive chemotherapeutic regimens with a three-drug combination were usually used in perioperative treatment or combined with radiotherapy. In the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial, the perioperative combination of three drugs consisting of epirubicin, cisplatin, and fluorouracil significantly improved progression-free survival and OS in patients with operable gastric or lower esophageal adenocarcinomas [12]. In the CALGB 80101 study, after curative resection of gastric or gastroesophageal junction adenocarcinoma, adjuvant chemoradiotherapy using the three-drug regimen of epirubicin, cisplatin, and infusional FU (ECF) did not improve survival compared with chemoradiotherapy with bolus fluorouracil and leucovorin [13]. A multicenter randomized phase □ trial (NCT02931890) of neoadjuvant docetaxel, oxaliplatin, plus capecitabine chemotherapy with or without radiotherapy in resectable gastric cancer had been initiated, and the results were as expected [14]. To our knowledge, our study is the first attempt to evaluate the triple-drug combination with taxanes as adjuvant chemotherapy for patients who underwent curative gastrectomy.

In this study, extended lymphadenectomy, also known as D2 gastrectomy, was carried out in only 47% of patients, similar to that of the MAGIC study, whereas in the CLASSIC and ACTS-GC trials, all patients underwent gastrectomy plus D2 gastrectomy. In fact, in the actual clinical practice, D1 lymphadenectomy is still performed by some surgeons. According to the INT-0116 study [15], of which D2 surgery was performed in only 10% of patients with gastric or gastroesophageal adenocarcinoma, postoperative chemoradiotherapy should be considered. However, our patients received adjuvant chemotherapy alone, but not radiation. In view of this fact and taking into account that postoperative chemoradiotherapy using the triple ECF regimen did not provide survival benefit in the CALGB 80101 study [13], we postulated that the omission of postoperative radiation may partially explain the overlap of survival curves for the two groups.

Due to the limitations in terms of data acquisition and the retrospective design of the study, treatment-related toxicity could not be detected in our study; as typically known, patients undergoing intensive chemotherapy may experience greater toxicities, and this could influence the efficacy of the adjuvant chemotherapy. In addition, some important information cannot be obtained in our study, for example, nutritional status after surgery, comorbidity, and postoperative complications et al. [16-20], These factors were considered to have an influence on the survival of the patients.

Conclusions

We concluded that adjuvant chemotherapy with taxanes, platinum and fluoropyrimidines for stage □-□ gastric adenocarcinoma after curative gastrectomy did not show survival benefit compared to doublet regimen of platinum and fluoropyrimidines. Further optimization of adjuvant treatment for gastric cancer patients who underwent curative surgery could improve patient survival, and prospective randomized trials should be conducted to assess the efficacy of taxanes in the adjuvant setting.

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of the First Affiliated Hospital of Anhui Medical University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent for publication: Not applicable.

Availability of data and materials: The data that support the findings of this study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by LW, ZW and HX. The first draft of the manuscript was written by LW and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A: **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries**. *CA Cancer J Clin* 2018, **68**(6):394-424.
2. Kim lH: **Current status of adjuvant chemotherapy for gastric cancer**. *World J Gastrointest Oncol* 2019, **11**(9):679-685.
3. Noh SH, Park SR, Yang HK, Chung HC, Chung IJ, Kim SW, Kim HH, Choi JH, Kim HK, Yu W *et al*: **Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial**. *Lancet Oncol* 2014, **15**(12):1389-1396.
4. Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, Nashimoto A, Fujii M, Nakajima T, Ohashi Y: **Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer**. *J Clin Oncol* 2011, **29**(33):4387-4393.

5. Tsuburaya A, Yoshida K, Kobayashi M, Yoshino S, Takahashi M, Takiguchi N, Tanabe K, Takahashi N, Imamura H, Tatsumoto N *et al*: **Sequential paclitaxel followed by tegafur and uracil (UFT) or S-1 versus UFT or S-1 monotherapy as adjuvant chemotherapy for T4a/b gastric cancer (SAMIT): a phase 3 factorial randomised controlled trial**. *Lancet Oncol* 2014, **15**(8):886-893.
6. Yoshida K, Kodera Y, Kochi M, Ichikawa W, Kakeji Y, Sano T, Nagao N, Takahashi M, Takagane A, Watanabe T *et al*: **Addition of Docetaxel to Oral Fluoropyrimidine Improves Efficacy in Patients With Stage III Gastric Cancer: Interim Analysis of JACCRO GC-07, a Randomized Controlled Trial**. *J Clin Oncol* 2019, **37**(15):1296-1304.
7. Al-Batran SE, Homann N, Pauligk C, Illerhaus G, Martens UM, Stoehlmacher J, Schmalenberg H, Luley KB, Prasnikar N, Egger M *et al*: **Effect of Neoadjuvant Chemotherapy Followed by Surgical Resection on Survival in Patients With Limited Metastatic Gastric or Gastroesophageal Junction Cancer: The AIO-FLOT3 Trial**. *JAMA Oncol* 2017, **3**(9):1237-1244.
8. Shah MA, Janjigian YY, Stoller R, Shibata S, Kemeny M, Krishnamurthi S, Su YB, Ocean A, Capanu M, Mehrotra B *et al*: **Randomized Multicenter Phase II Study of Modified Docetaxel, Cisplatin, and Fluorouracil (DCF) Versus DCF Plus Growth Factor Support in Patients With Metastatic Gastric Adenocarcinoma: A Study of the US Gastric Cancer Consortium**. *J Clin Oncol* 2015, **33**(33):3874-3879.
9. Van Cutsem E, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, Rodrigues A, Fodor M, Chao Y, Voznyi E *et al*: **Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group**. *J Clin Oncol* 2006, **24**(31):4991-4997.
10. Wang J, Xu R, Li J, Bai Y, Liu T, Jiao S, Dai G, Xu J, Liu Y, Fan N *et al*: **Randomized multicenter phase III study of a modified docetaxel and cisplatin plus fluorouracil regimen compared with cisplatin and fluorouracil as first-line therapy for advanced or locally recurrent gastric cancer**. *Gastric Cancer* 2016, **19**(1):234-244.
11. Lu Z, Zhang X, Liu W, Liu T, Hu B, Li W, Fan Q, Xu J, Xu N, Bai Y *et al*: **A multicenter, randomized trial comparing efficacy and safety of paclitaxel/capecitabine and cisplatin/capecitabine in advanced gastric cancer**. *Gastric Cancer* 2018, **21**(5):782-791.
12. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, Scarffe JH, Lofts FJ, Falk SJ, Iveson TJ *et al*: **Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer**. *N Engl J Med* 2006, **355**(1):11-20.
13. Fuchs CS, Niedzwiecki D, Mamon HJ, Tepper JE, Ye X, Swanson RS, Enzinger PC, Haller DG, Dragovich T, Alberts SR *et al*: **Adjuvant Chemoradiotherapy With Epirubicin, Cisplatin, and Fluorouracil Compared With Adjuvant Chemoradiotherapy With Fluorouracil and Leucovorin After Curative Resection of Gastric Cancer: Results From CALGB 80101 (Alliance)**. *J Clin Oncol* 2017, **35**(32):3671-3677.
14. Slagter AE, Jansen EPM, van Laarhoven HWM, van Sandick JW, van Grieken NCT, Sikorska K, Cats A, Muller-Timmermans P, Hulshof M, Boot H *et al*: **CRITICS-II: a multicentre randomised phase II trial of**

neo-adjuvant chemotherapy followed by surgery versus neo-adjuvant chemotherapy and subsequent chemoradiotherapy followed by surgery versus neo-adjuvant chemoradiotherapy followed by surgery in resectable gastric cancer. *BMC Cancer* 2018, **18**(1):877.

15. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, Haller DG, Ajani JA, Gunderson LL, Jessup JM *et al*: **Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction**. *N Engl J Med* 2001, **345**(10):725-730.
16. Zhao B, Zhang J, Zhang J, Zou S, Luo R, Xu H, Huang B: **The Impact of Preoperative Underweight Status on Postoperative Complication and Survival Outcome of Gastric Cancer Patients: A Systematic Review and Meta-analysis**. *Nutr Cancer* 2018, **70**(8):1254-1263.
17. Ryo S, Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, Murai T, Asada T, Ishiyama A, Matsushita H *et al*: **The Controlling Nutritional Status Score Serves as a Predictor of Short- and Long-Term Outcomes for Patients with Stage 2 or 3 Gastric Cancer: Analysis of a Multi-institutional Data Set**. *Ann Surg Oncol* 2019, **26**(2):456-464.
18. Maezawa Y, Aoyama T, Kano K, Tamagawa H, Numata M, Hara K, Murakawa M, Yamada T, Sato T, Ogata T *et al*: **Impact of the Age-adjusted Charlson comorbidity index on the short- and long-term outcomes of patients undergoing curative gastrectomy for gastric cancer**. *J Cancer* 2019, **10**(22):5527-5535.
19. Gertsen EC, Goense L, Brenkman HJF, van Hillegersberg R, Ruurda JP, Dutch Upper Gastrointestinal Cancer Audit g: **Identification of the clinically most relevant postoperative complications after gastrectomy: a population-based cohort study**. *Gastric Cancer* 2019.
20. Yuan P, Wu Z, Li Z, Bu Z, Wu A, Wu X, Zhang L, Shi J, Ji J: **Impact of postoperative major complications on long-term survival after radical resection of gastric cancer**. *BMC Cancer* 2019, **19**(1):833.

Tables

Table 1. Characteristics of patients in PF group and TPF group.

Variables	PF group [*n*(%), *n*=112]	TPF group [*n*(%), *n*=44]	*χ2*	*P*
Age (ys)			1.399	0.237
<65	73 (65.2)	33 (75.0)		
65+	39 (34.8)	11 (25.0)		
Sex			0.015	0.904
Male	80 (71.4)	31 (70.5)		
Female	32 (28.6)	13 (29.5)		
Tumor location			0.374	0.541
Cardia	57 (50.9)	20 (45.5)		
Non-cardia	55 (49.1)	24 (54.5)		
Borrmann subtype			0.158	0.691
/	42 (37.5)	15(34.1)		
/	70 (62.5)	29 (65.9)		
Grade			0.002	0.969
G1-2	36 (32.1)	14 (31.8)		
G3-4	76 (67.9)	30 (68.2)		
T stage (AJCC 7th)			1.599	0.449
T1-2	9 (8.0)	4 (9.1)		
T3	73 (65.2)	24 (54.5)		
T4	30 (26.8)	16 (36.4)		
N stage (AJCC 7th)			4.141	0.247
N0	13 (11.6)	1 (2.3)		
N1	29 (25.9)	10 (22.7)		
N2	35 (31.3)	15 (34.1)		
N3	35 (31.3)	18 (40.9)		
Stage (AJCC 7th)			3.041	0.081
	36 (32.1)	8 (18.2)		
	76 (67.9)	36 (81.8)		
Vascular invasion			0.544	0.461
Yes	22 (19.6)	11 (25.0)		
No	90 (80.4)	33 (75.0)		
Perineuronal invasion			0.547[a]	0.460
Yes	14 (12.5)	3 (6.8)		
No	98 (87.5)	41 (93.2)		
Tumor deposits			0.036	0.848
Positive	14 (12.5)	6 (13.6)		
Negative	98 (87.5)	38 (86.4)		
Unfavorable pathological factors[b]			0.155	0.694
Yes	42 (37.5)	18 (40.9)		
None	70 (62.5)	26 (59.1)		
Laparotomic approaches			0.365	0.546
Open laparotomy	101 (91.0)	42 (95.5)		
Laporascopy	10 (9.0)	2 (4.5)		
Scope of gastrectomy			1.048	0.306
Total gastrectomy	83 (74.1)	29 (65.9)		
Partial gastrectomy	29 (25.9)	15 (34.1)		
Lymph nodes dissection			0.002	0.964
D1	59 (52.7)	23 (52.3)		
D2	53 (47.3)	21 (47.7)		

[a]Continuity correction *χ2*; [b]Patients with either microscopic residues, or vessel invasion, or perineuronal invasion or tumor node in postoperative samples.

Table 2. Details of adjuvant chemotherapy in the PF group and TPF group.

	PF group [*n*(%), *n*=112]	TPF group [*n*(%), *n*=44]	χ^2	*P*
Paclitaxel	—	22 (50)	—	—
Docetaxel	—	22 (50)	—	—
5-Fu[a]	62 (55.4)	30 (68.2)	2.147	0.143
Capecitabine[a]	33 (29.5)	11 (25.0)	0.311	0.577
S1[a]	26 (23.2)	11 (25.0)	0.056	0.813
Cisplatin[b]	3 (2.7)	25 (56.8)	62.872	0.000
Oxaliplatin[b]	105 (93.8)	25 (56.8)	31.023	0.000
Lobaplatin[b]	8 (7.1)	4 (9.1)	0.006[c]	0.939
Time to chemotherapy after surgery (days, median [P25, P75])	37 [30, 44]	38 [32, 45]	—	0.322[d]
Duration of adjuvant chemotherapy (days, median [P25, P75])	127 [67, 157]	134 [82, 174]	—	0.265[d]
Cycles of adjuvant chemotherapy (median [P25, P75])	5[3, 6]	5[3, 6]	—	0.671[d]

[a]Some patients switched to another fluoropyrimidines compounds in different cycles due to side effects or other considerations; [b]Some patients switched to another platinum compounds in different cycles due to side effects or other considerations; [c]Continuity correction χ^2; [d]Independent samples Mann-Whitney U test.

Figures

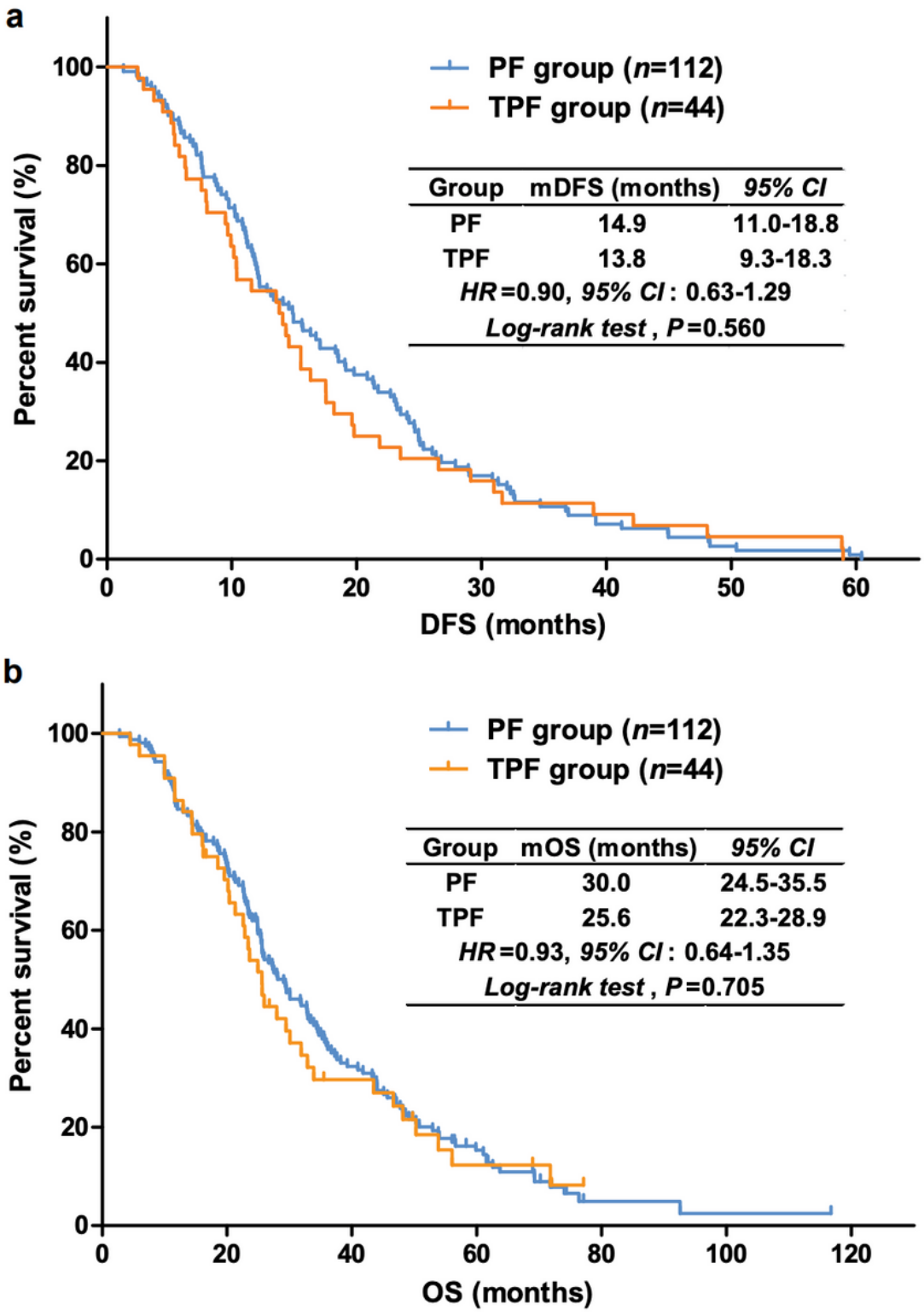

Figure 1

Kaplan-Meier disease-free survival (DFS) and overall survival (OS) curves for the gastric cancer patients with adjuvant chemotherapy. a, DFS curves; b, OS curves; PF, platinum plus fluoropyrimidines; TPF, taxanes, platinum plus fluoropyrimidines; HR, hazard ratio

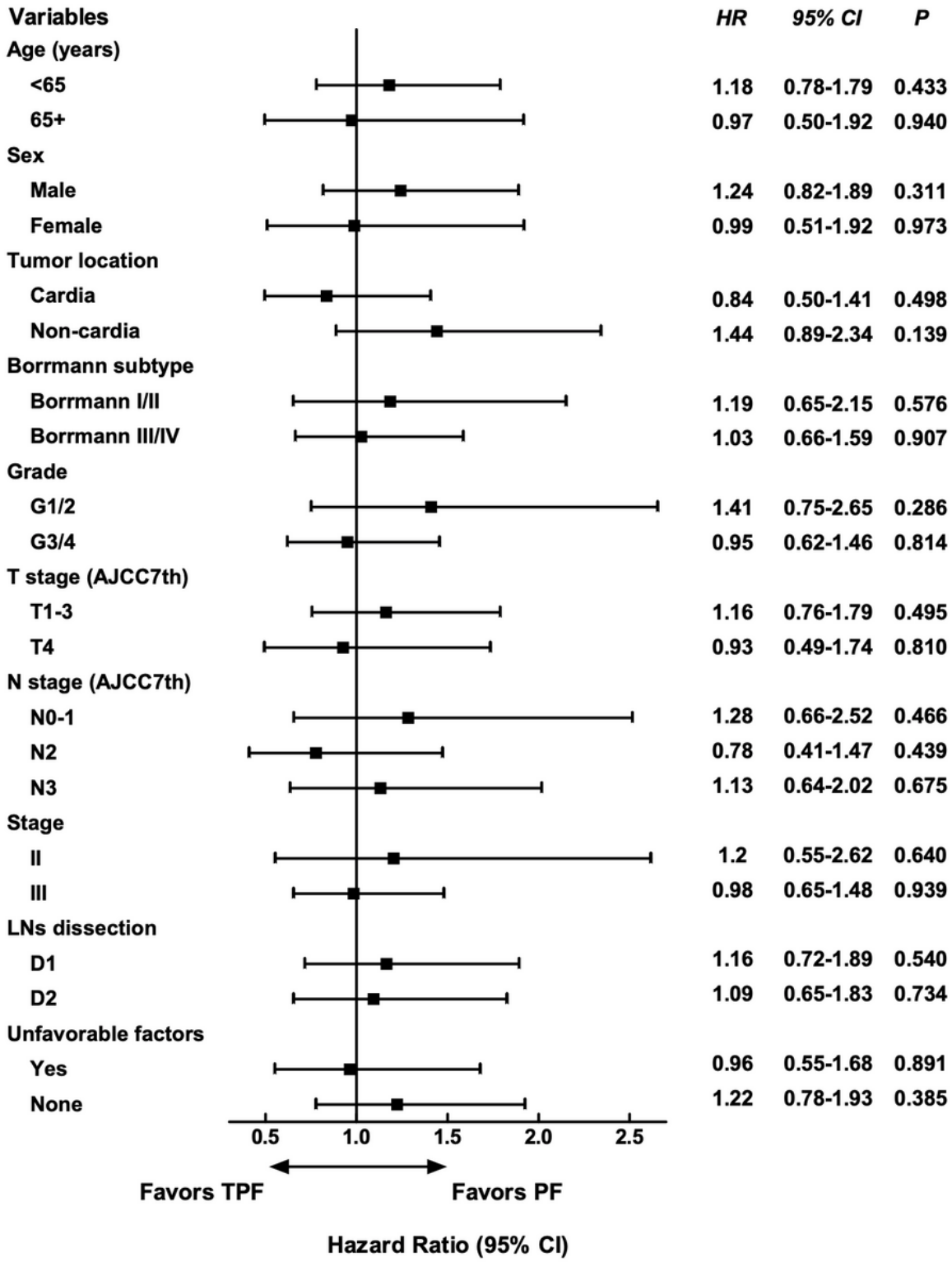

Figure 2

Disease-free survival hazard ratios (taxanes, platinum plus fluoropyrimidines over platinum plus fluoropyrimidines) of the two groups according to baseline characteristics. Results were based on Cox-adjusted analyses. PF, platinum plus fluoropyrimidines; TPF, taxanes, platinum plus fluoropyrimidines; LNs, lymph nodes; HR, hazard ratio

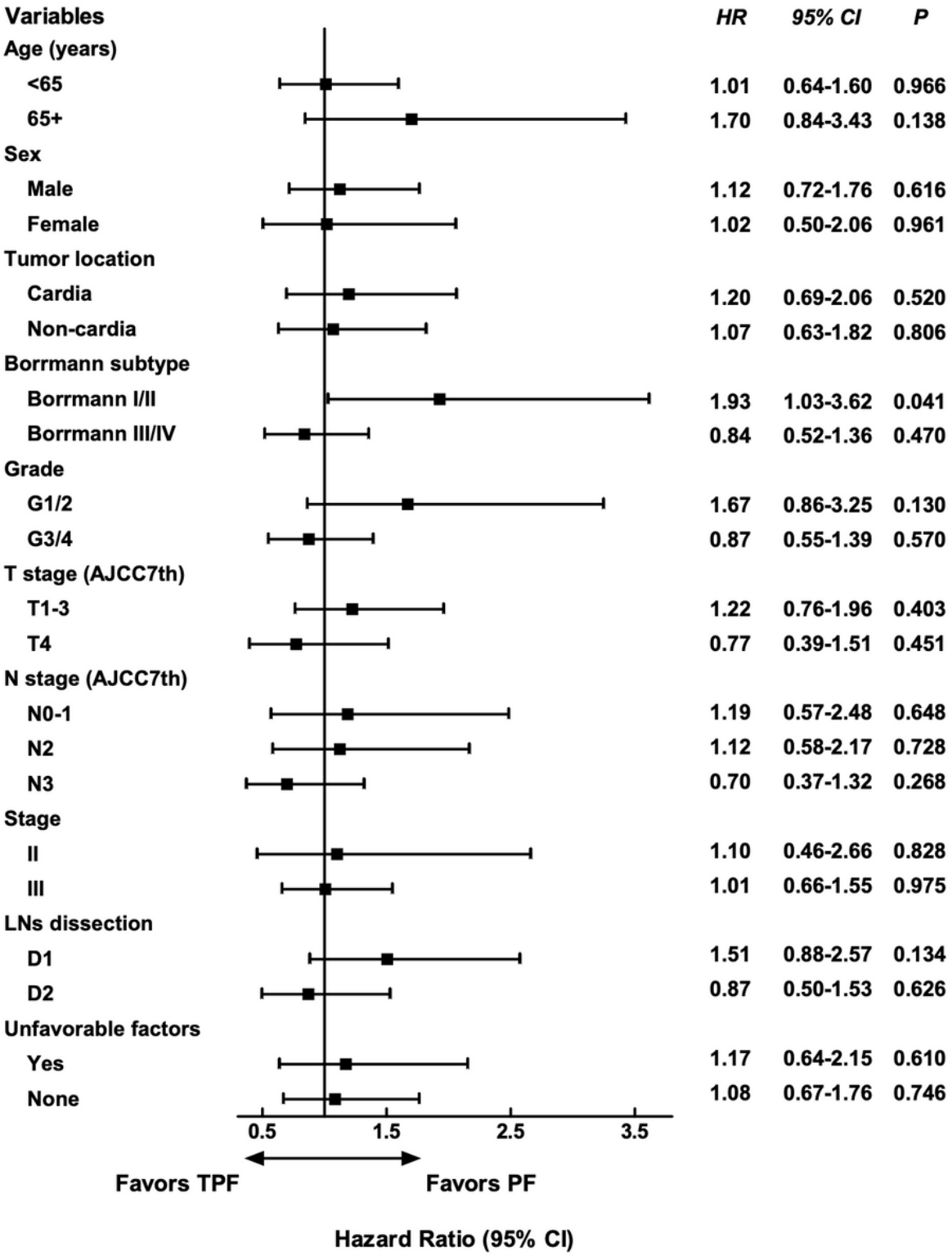

Figure 3

Overall survival hazard ratios (taxanes, platinum plus fluoropyrimidines over platinum plus fluoropyrimidines) of the two groups according to baseline characteristics. Results were based on Cox-adjusted analyses. PF, platinum plus fluoropyrimidines; TPF, taxanes, platinum plus fluoropyrimidines; LNs, lymph nodes; HR, hazard ratio