

Transthoracic Approach vs Transhiatal-Abdominal Approach in the Treatment of Locally Advanced Siewert Type II Esophagogastric Junctional Adenocarcinoma: A Retrospective Study

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Research Article

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Abstract

Background The surgical approach for Siewert type II adenocarcinoma of the esophagogastric junction still remains controversial. This study aims to compare the differences between transthoracic approach and transhiatal-abdominal approach.

Methods Patients with Siewert type II adenocarcinoma of the esophagogastric junction underwent surgery from January 2010 to July 2015 were analyzed retrospectively. They were divided into transthoracic approach group and transhiatal-abdominal approach group. Postoperative complications, surgical characteristics and 5-year survival rates of the two groups were compared by Chi-square test and log-rank test respectively, and the extent of gastrectomy was analyzed in subgroups. Finally, Cox univariate and multivariate analyses were conducted to predict the independent prognostic factors for long-term survival.

Result A total of 255 patients with Siewert type II adenocarcinoma of the esophagogastric junction were analyzed, 143 with transthoracic approach group, 112 with transhiatal-abdominal approach group and the 5-year survival rate was 37.8% and 40.2% respectively ($P=0.575$). The incidence of positive proximal margins (0.70% vs. 6.25%, $P=0.023$) and intraoperative bleeding volume (175.15 ± 110.44 vs. 206.57 ± 131.97 ml, $P=0.046$) in transthoracic approach group were lower. Transhiatal-abdominal approach group had fewer pulmonary infection (8.04% vs. 17.48%, $P=0.028$) and shorter hospitalization time (11.32 vs. 12.67 days, $P=0.008$). In subgroup analysis, the 5-year survival rate of patients treated with partial gastrectomy was better than that of patients treated with total gastrectomy (44.8% vs. 36.1%, $P=0.038$).

Conclusion Our study shows no significant difference between the two groups with regard to long-term survival. The transthoracic approach had more advantages for proximal margin and mediastinal lymph node dissection, while the transabdominal approach had less trauma to patients. Partial gastrectomy may be sufficient for patients with locally advanced disease. T stage and N stage were independent risk factors for long-term survival.

Introduction

Esophagogastric junction cancer refers to the carcinoma with an epicenter located within the range of 5 cm above and below the esophagogastric junction and crosses or contacts the dentate line(1). There were about 260,000 patients globally in 2012(2). Among them, east and Southeast Asia accounted for 59%, more than half of the cases occurred in China, and adenocarcinoma of the esophagogastric junction (AEG) was the main pathologic type. Siewert et al(3) classified AEG into three types according to anatomic location. AEG I refers to the carcinoma with an epicenter located within 1 to 5 cm above the dentate line, AEG II to the carcinoma with an epicenter located within the range from 1 cm above to 2 cm below the dentate line and AEG III to the carcinoma with an epicenter located within 2 to 5 cm below the dentate line.

AEG is mainly treated by surgery. Transthoracic esophagectomy plus adequate mediastinal lymph node dissection are adopted for AEG I, whereas total gastrectomy and transhiatal distal esophagectomy with lower mediastinal and abdominal (D2) node dissection are used for AEG III. As for AEG II, which crosses the dentate line, is quite different from the other two types in terms of pathological source and lymphatic drainage direction(4–6). To date, the choice of transthoracic or transhiatal-abdominal as the surgical approach remains in debate(7–9). The aim of this retrospective observational single-center study is to analyze clinicopathological data for transthoracic and transhiatal-abdominal approaches at Anhui Provincial Hospital and compare postoperative complications, surgical characteristics and long-term survival rates between the two.

Methods

Patients

From January 2010 to July 2015, 942 patients with esophagogastric junction cancer underwent surgery at Anhui Provincial Hospital. The inclusion criteria were as follows: (I) locally advanced AEG II (T2, T3, T4); (II) no prior neoadjuvant chemo-/chemoradiotherapy before surgery; and (III) no distant metastasis. The exclusion criteria were (I) incomplete clinicopathological data or loss to follow-up, (II) palliative surgery or exploratory surgery, and (III) other malignant diseases. In total, 255 patients were enrolled, including 143 in the transthoracic approach group (TT group) and 112 in the transhiatal-abdominal approach group (TH group). Pathological staging was carried out according to the eighth edition of the TNM staging system(10). The present study is performed in accordance with the Declaration of Helsinki (as revised in 2013), Good Clinical Practice, and related laws.

Surgical procedure

The transthoracic approach was performed with proximal gastrectomy and distal esophagectomy from a lateral incision between the 7th and 8th ribs of the left-side chest, followed by esophagogastrotomy. The supradiaphragmatic lymph nodes, lower paraesophageal lymph nodes and subcarinal lymph nodes in the mediastinum and the perigastric lymph nodes in the abdomen were cleaned. In some patients, a left thoracoabdominal approach consisting of total gastrectomy and D2 lymphadenectomy, followed by esophagojejunostomy Roux-en-Y intrathoracic anastomosis was applied. The transhiatal-abdominal approach was performed with distal esophagectomy through the esophageal hiatus, followed by proximal or total gastrectomy and then esophagogastric anastomosis or Roux-en-Y esophagojejunostomy. D2 lymph node dissection was adopted for total gastrectomy and D1+ lymph node dissection for proximal gastrectomy.

Follow-up observation

Patients were followed up via phone calls or hospital visits to track their postoperative therapy status, survival status, survival time and quality of life after surgery. Overall survival (OS) was defined as the time from surgery to death or the last day of follow-up, which was October 01, 2020.

Statistical analysis

All statistical analyses were performed using the software SPSS 19.0. Continuous variables are expressed as the mean \pm standard deviation ($\bar{x} \pm s$) and categorical variables as percentages. Continuous variables were compared by the t-test; categorical variables were compared using χ^2 test or Fisher's exact test. Survival curves were derived from Kaplan-Meier estimates and compared by using the log-rank test. Prognostic factors were identified by univariate analysis. Factors with statistical significance ($P < 0.05$) were further analyzed by a Cox proportional-hazards model. We considered $P < 0.05$ as statistically significant.

Table 1
Correlation of the clinicopathological characteristics between the TT and TH group

Clinicopathological characteristics	TT(n=143)	TH(n=112)	P
Age(years,mean±SD)	64.78±7.70	64.08±7.90	0.480
Gender (Male/Female)	118(82.52%)/25(17.48%)	88(78.57%)/24(21.43%)	0.427
Histological differentiation			0.452
High	3(2.10%)	1 (0.89%)	
Mid	63(44.06%)	43(38.39%)	
Poor	77(53.85%)	68 (60.71%)	
Postoperative adjuvant chemotherapy (yes/no)	54(37.76%)/89(62.24%)	48(42.86%)/64(57.14%)	0.410
TNM stage			0.269
1	10 (6.99%)	5 (4.46%)	
2	34 (23.78%)	30 (26.79%)	
3	61 (42.66%)	57 (50.89%)	
4	38 (26.57%)	20 (17.86%)	
T stage			0.087
2	24 (16.78%)	16 (14.29%)	
3	97 (67.83%)	88 (78.57%)	
4	22 (15.38%)	8 (7.14%)	
N stage			0.239
0	46 (32.17%)	36 (32.14%)	
1	30 (20.98%)	32 (28.57%)	
2	32 (22.38%)	27 (24.11%)	
3	35 (24.48%)	17 (15.18%)	

Results

The clinicopathological characteristics of the two groups are shown in Table 1. The baseline between groups was comparable. In subgroup analysis, the TNM stage was significantly later in those undergoing total gastrectomy than in those undergoing partial gastrectomy ($P < 0.001$, Table 2).

Morbidity and mortality

Postoperative complications and mortality are provided in Table 3. The incidence of pulmonary infection in the TT group was significantly higher than that in the TH group (17.48% vs. 8.04%, P = 0.028). In contrast, there was no significant difference in grade III-IV complications (based on the Clavien-Dindo grading system) or perioperative mortality between the two groups.

Table 2

Correlation of the clinicopathological characteristics between patients with total and partial gastrectomy

Clinicopathological characteristics	PG(n=142)	TG(n=113)	P
Age(years, mean±SD)	109(76.76%)/33(23.24%)	97(85.84%)/16(14.16%)	0.068
Histological differentiation			0.189
High	2 (1.41%)	2 (1.77%)	
Mid	66 (46.48%)	40 (35.40%)	
Poor	74 (52.11%)	71 (62.83%)	
Postoperative adjuvant chemotherapy (yes/no)	58(40.85%)/84(59.15%)	44(38.94%)/69(61.06%)	0.757
TNM stage			<0.001
1	12 (8.45%)	3 (2.65%)	
2	40 (28.17%)	24 (21.24%)	
3	66 (46.48%)	52 (46.02%)	
4	24 (16.90%)	34 (30.09%)	
T stage			<0.001
2	35 (24.65%)	5 (4.42%)	
3	92 (64.79%)	93 (82.30%)	
4	15 (10.56%)	15 (13.27%)	

Table 3
Postoperative morbidity and mortality between two groups

Variable	TT(n=143)	TH(n=112)	P
Total complications	41(28.67 %)	26(23.21%)	0.326
Clavien-Dindo Grade (Grade 2)	32(22.38%)	21(18.75%)	0.479
Pulmonary infection	25(17.48%)	9(8.04%)	0.028
arrhythmia	2(1.40%)	2(1.79%)	1.000
Abdominal infection	0	3(2.68%)	0.083
Chylothorax	1(0.70%)	0	1.000
Gastrointestinal dysfunction	1(0.70%)	3(2.68%)	0.323
Hypoproteinemia	2(1.40%)	2(1.79%)	1.000
Wound infection	1(0.70%)	2(1.79%)	0.584
Clavien-Dindo Grade (Grade 3-4)	9(6.29%)	5(4.46%)	0.524
Abdominal haemorrhage	0	2(1.79%)	0.192
Respiratory failure	2(1.40%)	1(0.89%)	1.000
Chylothorax	5(3.50%)	2(1.79%)	0.471
Liver and kidney failure	1(0.70%)	0	1.000
Pulmonary embolism	1(0.70%)	0	1.000
30-days mortality	1(0.70%)	2(1.79%)	0.584

Surgical characteristics

Surgery-related characteristics are listed in Table 4. Positive proximal margin (0.7% vs. 6.25%, $P < 0.05$) and bleeding volume (175.15 ± 110.44 vs. 206.57 ± 131.97 ml, $P = 0.046$) rates in the TT group were lower than those in the TH group. However, postoperative hospitalization time was shorter in the TH group than in the TT group (11.32 ± 3.68 vs. 12.67 ± 4.04 days, $P = 0.008$). Nevertheless, there was no significant difference in the total number of lymph nodes dissected and celiac lymph nodes dissected between the groups. Although the total number of lymph node dissections was slightly higher in the TT group than in the TH group (15.47 ± 6.92 vs. 13.93 ± 5.92 , $P = 0.062$), the opposite result was found for the number of lymph nodes dissected in the abdominal cavity (TH 13.49 ± 5.82 vs. TT 12.16 ± 5.89 , $P = 0.073$). The average number of thoracic lymph nodes in the TT group was 2.75; these lymph nodes were rarely cleaned in TH group. Finally, the celiac lymph node metastasis rate in the TT and TH groups was 62.9% and 68.8%, respectively ($P = 0.333$), and the thoracic lymph node metastasis rate was 14.7% in the TT group.

Table 4
Comparison of the different surgery-related characteristics between the TT and TH group

Variable	TT(n=143)	TH(n=112)	P
Total number of removed lymph nodes	15.47±6.92	13.93±5.92	0.062
Number of removed lymph node in abdomen	12.16±5.89	13.49±5.82	0.073
Number of removed lymph node in thorax	2.75±3.43	0.06±0.34	<0.001
MLR in abdomen	90(62.9%)	77(68.8%)	0.333
MLR in thorax	21(14.69%)	-	-
Blood loss	175.15±110.44	206.57±131.97	0.046
Proximal margin status (Positive/Negative)	1(0.70%)/142(99.30%)	7(6.25%)/105(93.75%)	0.023
Postoperative hospital stay (d)	12.67±4.04	11.32±3.68	0.008

MLR (Metastatic lymph node ratio) = number of patients with positive lymph nodes /the number of patients collected in the station

Survival and prognostic factors

The 5-year OS rates in the TT group, TH group and the entire study cohort were 37.8%, 40.2% and 38.8%, respectively. No significant difference in terms of OS between the two groups was found (Fig. 1-A). In subgroup analysis, the 5-year OS rates of patients undergoing transthoracic total gastrectomy and transhiatal-abdominal total gastrectomy were 26.1% and 34.7%, respectively (Fig. 1-B). The 5-year OS of patients undergoing transthoracic partial gastrectomy and transhiatal-abdominal partial gastrectomy was 42.7% and 50%, respectively (P=0.349, Fig. 1-C), that of patients undergoing transthoracic total and partial gastrectomy was 26.1% and 42.7%, respectively (P=0.069, Fig. 1-D), and that of patients undergoing transhiatal-abdominal total and partial gastrectomy was 34.7% and 50.0%, respectively (P=0.116, Fig. 1-E), all with no significant difference. In subgroup analysis, the 5-year OS rate of patients treated with partial gastrectomy was significantly higher than that of patients treated with total gastrectomy (44.8% vs. 36.1%, P=0.038, Fig. 1-F). Moreover, multivariate analysis of survival showed that T and N stage was an independent risk factor for prognosis (P < 0.05) but that age, sex, gastrectomy and surgical approach had no significant impact on the long-term survival of patients (Table 5).

Discussion

The mainstay treatment of AEG II is surgery(11, 12), but the choice of surgical approach, the scope of lymph node dissection and the optimal extent of gastrectomy are still debatable(8, 9, 13). We conducted

this study to analyze the different outcomes of surgical-related characteristics and survival rate between the transthoracic and transhiatal-abdominal approaches to explore optimal treatment for AEG II.

It has been reported that the incidence of postoperative complications of a transthoracic approach for AEG II is significantly higher than that of a transabdominal approach(7, 14, 15). In our study, the incidence of complications was significantly higher in the TT group than in the TH group (17.48% vs. 8.04%, $P = 0.028$), which may be explained by the fact that the transthoracic approach leads to more mechanical lung injury. In accordance with some previous work(15, 16), there was no significant difference in the incidence of other grade II complications or in anastomotic fistula and other serious complications (grade III-IV) between the two groups. Consequently, the 30-day postoperative mortality was not significantly different between the groups, indicating a similar safety with these two surgical approaches for AEG II.

Lymphatic drainage in AEG II occurs simultaneously to the thoracic cavity and abdominal cavity due to the location(17, 18). Previous studies have shown that a sufficient number and extent of lymph node dissection are independent risk factors affecting the long-term survival of patients(19, 20). Some studies have suggested that the transhiatal-abdominal approach can remove more lymph nodes(7, 21), though other studies have reported no difference between them(22). In this study, the total number of lymph nodes dissected in the TT group was slightly higher than that in the TH group, but with no significant difference, indicating that for total lymph node cleaning efficiency, the two surgical approach are essentially similar. In general, it is relatively difficult to dissect lymph nodes along the celiac artery, splenic artery and common hepatic artery with the transthoracic approach, especially the traditional left transthoracic approach, though middle and lower mediastinal lymph nodes are accessible. In this study, the thoracic lymph node metastasis rate in the TT group was 14.7%, indicating that mediastinal lymph node dissection is necessary for AEG II surgery.

The incidence of positive proximal margins in the TH group was significantly higher than that in the TT group. This result was consistent with Parry K et al(23), suggesting that the transthoracic approach is related to a higher average resection length of the esophagus and R0 resection rate(24). Combined with previous reports(24, 25), the transthoracic approach appears to be suitable with esophageal invasion of 3 cm or more for AEG II. In the present study, the hospitalization time of patients undergoing the transhiatal-abdominal approach was shorter than that of patients undergoing transthoracic surgery, consistent with previous reports(7, 8). These findings indicate that compared with the transthoracic approach, the transabdominal approach involves less trauma, less influence on respiratory function and faster recovery. Therefore, the transabdominal approach is more suitable for patients in a relatively poor general condition, especially those with poor pulmonary function.

Table 5: Survival related multivariate analysis

Variable	5-year survival related factors		P	multivariate analysis		P
	HR	CI 95%		HR	CI 95%	
Gender (Male vs Female)	1.255	(0.817-1.926)	0.299	-	-	-
Age (>=65 VS <65)	1.238	(0.901-1.702)	0.187	-	-	-
T stage						
2(reference)	1	-	-	1	-	-
3	3.396	(1.779-6.480)	<0.001	1.997	(1.010-3.948)	0.047
4	6.919	(3.314-14.447)	<0.001	3.234	(1.468-7.122)	0.004
N stage						
0(reference)	1	-	-	1	-	-
1	2.897	(1.768-4.747)	<0.001	2.506	(1.513-4.150)	<0.001
2	2.918	(1.759-4.840)	<0.001	2.436	(1.450-4.094)	0.001
3	6.927	(4.218-11.375)	<0.001	5.136	(3.042-8.671)	<0.001
Histological differentiation						
High(reference)	1	-	-	1	-	-
Mid	2.545	(0.352-18.394)	0.335	-	-	-
Poor	4.106	(0.572-29.454)	0.160	-	-	-
Gastrectomy (total/partial)	1.393	(1.014-1.913)	0.041	1.091	(0.789-1.509)	0.597
Surgery approach (TT/TH)	1.095	(0.795-1.507)	0.579	-	-	-
P < 0.05 in univariate analysis or previous research proved the variable related to prognosis were included in multivariate analysis						

Overall, the influence of a surgical approach on the long-term survival of patients is an important factor to evaluate its rational use, and results in previous studies are controversial. For example, Susan et al(26) searched an institutional prospectively maintained database and found the survival time of the transabdominal approach to be shorter than that of the right thoracoabdominal approach for AEG II, but this result may be related to the higher proportion of elderly patients over 70 years old in the transhiatal-abdominal approach group. The JCOG9502(16) study showed that the median survival time and five-year

survival rate of patients undergoing the transhiatal-abdominal approach were slightly higher than those of patients undergoing the left thoracoabdominal approach, but with no significant difference. In addition, Parry K et al(23) reported no difference in five-year survival rate between the transhiatal-abdominal and transthoracic approach, similar to our results. Indeed, subgroup analysis of gastrectomy revealed no significant difference in five-year survival between the subgroups. Therefore, we hold the opinion that the long-term effects of transthoracic and transabdominal approaches are similar for the surgical treatment of AEG II.

The optimal extent of gastrectomy for Siewert type II AEG, including total and partial gastrectomy, is always selected according to tumor size, stage, location and surgeon's preference. Zhao et al(27) analyzed the effects of transhiatal-abdominal total and partial gastrectomy on patients and concluded that the latter may have a better five-year survival rate in AEG II patients at IA-III A stage and a tumor diameter less than 3 cm; for patients at later stages, the extent of gastrectomy had no significant impact on long-term prognosis. Similarly, we conclude that for locally advanced AEG II, patients who underwent partial gastrectomy had a higher five-year survival rate than those who underwent total gastrectomy (44.8% vs. 36.1%, $P = 0.038$). In subgroup analysis, we also found that patients treated with partial gastrectomy had a higher survival advantage than those treated with total gastrectomy. We believed this was related to the choice of surgical method, as the tumor stage of the patients treated with total gastrectomy was later. Survival-related multivariate analysis in this study showed T stage and N stage to be independent risk factors affecting the prognosis of AEG II patients, and we consider tumor stage as the main factor related to the survival of these patients.

This study is a single-center retrospective study. Although relatively strict screening conditions were set, there may be a certain degree of selection bias, and the qualified sample size was relatively small. A prospective study needs to be designed to obtain more objective results.

Conclusion

In conclusion, our study shows no significant difference between the transthoracic and transhiatal-abdominal approaches for AEG II patients with regard to the 5-year survival rate. Both approaches are comparably safe for AEG II. However, the transthoracic approach with partial gastrectomy is a better choice if proximal margins cannot be safely achieved (usually esophageal tumor extension of more than 3 cm), whereas the transhiatal-abdominal approach appears to be preferable for patients with a relatively poor general condition, especially those with poor pulmonary function, due to less trauma. Partial gastrectomy is sufficient compared with total gastrectomy for locally advanced AEG II. Finally, T stage and N stage are independent risk factors for survival in AEG II.

Abbreviations

adenocarcinoma of the esophagogastric junction
AEG

Transhiatal-abdominal approach
TH
transthoracic approach
TT
total gastrectomy
TG
partial gastrectomy
PG
transhiatal-abdominal partial gastrectomy
THPG
transhiatal-abdominal total gastrectomy
THTG
transthoracic partial gastrectomy
TTPG
transthoracic total gastrectomy
TTTG
Overall survival
OS
Metastatic lymph node ratio
MLR

Declarations

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Author Contributions:

Huan Li Xiaodong Zhu Xinpeng Zhou: data collection literature search

Huan Li: statistical analysis manuscript preparation

Xinyu Mei: study design, provision of materials and resources, data interpretation.

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Figures

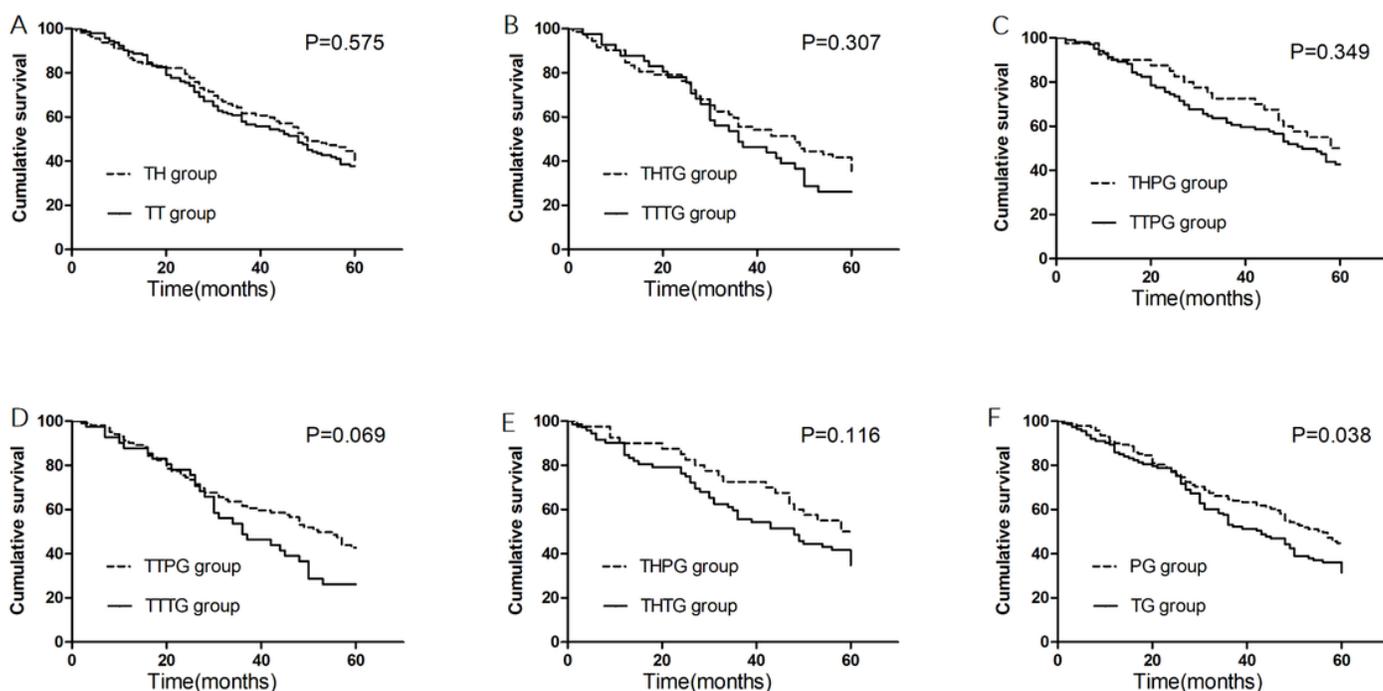


Figure 1

Fig 1-A, 5-year OS rate(TT 37.8% vs TH 40.2%, P=0.575);Fig 1-B, 5-year OS rate(TTTG 26.1% vs THTG 34.7%, P=0.307); Fig 1-C, 5-year OS rate (TTPG 42.7% vs THPG 50%, P=0.349); Fig 1-D, 5-year OS rate (TTTG 26.1% vs TTPG 42.7%, P=0.069); Fig 1-E, 5-year OS rate (THTG 34.7% vs THPG 50.0%, P=0.116); Fig 1-F, 5-year OS rate (PG 44.8% vs TG 36.1%, P=0.038);