

Surgical outcomes and survival for T4 gastric cancer extending to the transverse colon

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Research

Keywords: Stomach Neoplasms, Gastrectomy, Prognosis

Posted Date: February 7th, 2020

DOI: <https://doi.org/10.21203/rs.2.22878/v1>

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Version of Record: A version of this preprint was published at Annals of Translational Medicine on August 1st, 2020. See the published version at <https://doi.org/10.21037/atm-20-3377>.

Abstract

Purpose

Extended multi-organ resection for locally advanced (T4) gastric cancer remains controversial. Herein we aimed to evaluate the surgical outcomes and survival of patients with T4 gastric cancer extending to the transverse colon.

Materials and Methods

Between 2011 and 2015, forty patients had undergone curative resection for T4 gastric cancer extending to the transverse colon. Patient characteristics, related complications, long-term survival, and prognostic factors for T4 gastric cancer were analyzed.

Results

Post-operative morbidity occurred in 5 (12.5%) patients. The 1-, 3-, and 5-year overall survival rates were 75.0%, 49.2%, and 36.9%, respectively. Univariate analysis revealed that tumor size ($P = 0.049$), advanced T stage ($P = 0.013$), and lymph node metastasis ($P = 0.006$) are poor prognostic factors of overall survival. Based on multivariate analysis, advanced T stage and lymph node metastasis were identified as independent prognosis factors.

Conclusions

Patients with T4 gastric cancer extending to the transverse colon might benefit from curative resection with acceptable morbidity and mortality.

Background

Although the incidence of gastric cancer has decreased, gastric cancer remains the third leading cause of cancer-related death worldwide [1]. Currently, surgical resection is the most effective treatment for gastric cancer; however, once the tumor perforates the serosal layer and extends to the adjacent organs (T4), the prognosis is dismal. The 5-year overall survival rate of patients with T4 gastric cancer is < 20% and approximately 30% for patients who undergo surgery [2]. In such patients, radical gastrectomy with combined resection of involved organs is required. Nevertheless, extended resection of the involved organs leads to increased peri-operative morbidity and mortality. Therefore, choosing appropriate surgical strategy plays a key role for treating patients with T4 gastric cancer.

It has been reported that the transverse colon is one of the most frequently involved organs in patients with gastric cancer; however, few studies have focused on surgical outcomes and survival for T4 gastric cancer extending to the transverse colon. In the present study, we evaluated the surgical outcomes and survival of 40 patients with T4 gastric cancer extending to the transverse colon.

Materials And Methods

Between December 2011 and December 2015, a total of 2652 patients with gastric cancer underwent surgical treatment in the Department of General Surgery at our Hospital. Of these patients, 40 diagnosed with cT4b gastric cancer extending to the transverse colon were included in our study. This study was approved by the ethical committee of the hospital and informed consent was obtained from all of the patients. The inclusion criteria for the study were as follows: (1) age 18–75 years; (2) transverse colon involvement; and (3) R0 resection performed. R0 resection was defined as complete tumor removal with no macroscopically or microscopically residual tumor. Patients with peritoneal carcinomatosis and distant metastasis, and those who underwent resection of the distal esophagus and duodenum for expansion, splenectomy for lymph node dissection, and additional organ resections were excluded from the study.

All of the patients underwent gastrectomy with combined resection of the involved colon. Standard D2 lymph node dissections were performed in curative resection cases. A distal subtotal or total gastrectomy was performed depending on the location of the primary tumor. All patients were followed up once every 3 months for the first 2 years. At each follow-up visit, hematological tests and imaging studies (computed tomography [CT], magnetic resonance imaging, chest radiography, or ultrasonography) were carried out. The follow-up visits were extended to once every 6 months from 2 to 5 years and then to once every 12 months after 5 years.

Histologic classification and staging were based on the 8th edition of the International Union against Cancer (UICC) TNM classification. Histologic differentiations were classified into well- and poorly-differentiated categories.

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation (SD). For qualitative variables, the chi-square or Fisher's exact probability test was performed. For continuous variables, Student's t-test was applied. Survival was analyzed using the Kaplan-Meier method and survival comparisons between the groups were performed using the log-rank test. Cox regression multivariate analysis was used to identify the independent survival prognostic factors. A two-tailed P-value < 0.05 was considered to be statistically significant. Statistical analyses were performed with SPSS16.0.

Results

Of the 40 patients, 12 had tumors located in the middle third of the stomach, 22 had tumors located in the lower third of the stomach, and 6 had tumors involving the entire stomach. The tumor diameter ranged from 4–20 cm, with a mean diameter of 9 cm. Six patients received neoadjuvant chemotherapy, and a total of 31 patients received post-operative adjuvant chemotherapy.

The clinicopathologic features of the 40 patients are listed in Table 1. Twenty-nine patients were males and 11 were females. The mean age was 55.9 years, with a range between 42 and 75 years. Distal gastrectomies were performed in 15 patients, and total gastrectomies were performed in 25. Of the 40 patients, 22 had histologically-confirmed invasion to the transverse colon (pT4b), whereas 18 had only a desmoplastic reaction (pT4a). Twenty-nine patients (72.5%) had lymph node metastases, 12 (30.0%) had N1, 9 (22.5%) had N2, and 8 (20.0%) had N3 disease. Histologic evaluation revealed poorly-differentiated tumors in 33 patients, and well-differentiated tumors in 7 patients.

Table 1
Clinicopathologic features

Features	Value
Mean age (years)	55.9
Sex (male/female)	29/11
Tumor size (cm)	9.0 ± 5.0
Tumor location	
Middle	12
Lower	22
Whole	6
Histologic type	
Well differentiated	7
Poorly differentiated	33
Depth of invasion	
T4a	18
T4b	22
Lymph node involvement	
Negative	11
Positive	29
TNM stage	
II	5
III	35
Lymphatic invasion	
Yes	30
No	10
Vascular invasion	
Yes	9
No	31

Post-operative complications occurred in 5 patients. The rate of complications was 12.5%. Two patients developed anastomotic leakages, 1 developed an intra-abdominal infection, 1 developed a massive hydrothorax, and 1 developed a lung infection. All of the patients were cured with conservative treatment. No procedure-related mortality occurred.

The median follow-up period was 19 months (range, 7–69 months). The 1-, 3-, and 5-year overall survival rates were 75.0%, 49.2%, and 36.9%, with a median survival of 24 months. Tumor size (> 9 cm), advanced T stage, and lymph node metastasis were associated with poor survival based on univariate analysis (Table 2). Multivariate analysis demonstrated that advanced T stage and lymph node metastasis were independent prognosis factors for overall survival (Table 3). For patients with pT4a tumors, the overall survival rate at 3 years was 77.8%, whereas for patients with pT4b tumors, the overall survival rate at 3 years was 26.5% ($P = 0.013$; Fig. 1). The 3-year survival rate of patients with N0 was 77.8%, which was significantly better than patients with N+ ($P = 0.006$; Fig. 2). With respect to grade of lymph node metastasis, the patients with pN2 or greater tumors had significantly poorer 3-year survival than patients with pN1 tumors ($P = 0.027$; Fig. 3).

Table 2

Univariate prognostic analysis of survival in 40 patients with T4 gastric cancer

Features	n	3-year survival rate (%)	P value
Age (years)			
≤ 60	27	48.6%	0.555
> 60	13	53.8%	
Sex			
Male	29	48.4%	0.772
Female	11	45.5%	
Tumor size (cm)			
≤ 9.0	25	58.4%	0.049
>9.0	15	41.7%	
Histologic type			
Well differentiated	7	47.6%	0.638
Poorly differentiated	33	49.4%	
Depth of invasion			
pT4a	18	77.8%	0.013
pT4b	22	26.5%	
Lymph node metastasis			
No	11	77.8%	0.006
Yes	29	38.0%	
Grade of lymph node metastasis			
pN1	12	49.5%	0.027
pN2 ~ N3	17	-	
Lymphatic invasion			
Yes	30	47.4%	0.938
No	10	58.3%	
Vascular invasion			
Yes	9	-	0.301

Features	n	3-year survival rate (%)	P value
No	31	54.1%	

Table 3

Multivariate analysis of survival in 40 patients with T4 gastric cancer

Variable	Regression Coefficient	SE	Hazard ratio (95% CI)	P value
Tumor size	0.659	0.535	1.933(0.678 ~ 5.513)	0.218
Depth of invasion	1.294	0.606	3.646(1.112 ~ 11.955)	0.033
Lymph node metastasis	1.825	0.789	6.200(1.319 ~ 29.136)	0.021

SE = Standard Error.

Discussion

Gastric cancer is one of the most common cancers worldwide. Approximately 10% of patients have tumors that perforate the serosa and extend to adjacent organs [3, 4]. The transverse colon is the most common organ involved with gastric cancer; however, whether or not the patients with tumors invading the colon have improved survival than those with tumors invading other organs is still unknown. Some studies reported that there is no correlation between survival rate and which organ is invaded [5–7]. Pacelli et al. also found that patients with colon invasion had no survival advantage over those with other organ invasions [8]. Although Dhar et al. reported that patients with colon or mesocolon invasion had better survival rates than patients with other organ invasion based on univariate analysis; however, colon or mesocolon invasion was not a significant factor based on multivariate analysis [9]. These results indicated the prognosis of patients with invasion to the transverse colon was comparable to the prognosis of patients with invasion to other organs.

In our study, the 5-year overall survival rate was 36.9%, with a complication rate of 12.5%, which is considered acceptable. Fukuda et al. reported that the 5-year survival rate in T4 gastric cancer patients undergoing curative gastrectomy was 34.1% and the morbidity rate was 26.8% [4]. Brar et al. reviewed a total of 17 studies, including 1343 patients with locally advanced gastric cancer, and observed that the 5-year survival rate after R0 resection was 32%-35% and the overall complication rates ranged from 11.8%-90.5% [2]. In a recent study, the 3-year survival rate of 47.7% and complication rate of 37.9% were obtained from patients with clinical T4b gastric cancer [10]. Thus, the long-term outcomes in our study were similar to those in previous studies. However, we achieved a less complication rate compared with previous studies, which could be attribute to only colon resection in our study. Kasakura et al. found that patients with additional organs resection had a higher complication rate compared with patients undergoing gastrectomy alone [11], and Ozer et al. found that patients who underwent MVR with 2 or more organs had a higher surgical morbidity [12]. Based on these considerations, we suggest that

extended gastrectomy with involved colon resection can be performed with minimal morbidity and can improve the probability of overall survival in T4 gastric cancer extending to the transverse colon.

The most commonly reported prognostic factors of T4 gastric cancer patients are curability, the depth of tumor invasion, and lymph node metastasis. Curative resection offers the likelihood for cure, and non-curative resection is usually adopted in patients with peritoneal carcinomatosis and distant metastasis for palliative. Survival in patients who underwent multi-visceral resection without a complete resection was demonstrated to be significantly diminished compared to those patients had R0 resections [13, 14]. Dhar et al. treated 150 patients with T4 gastric cancer and reported that curative patients had survival benefit over non-curative patients [9]. Furthermore, Mita et al. concluded that extended multi-organ resection could be beneficial only if curative surgery was performed [15]. Therefore, our study was limited to patients without distant metastasis who were treated with curative resection. Our results further demonstrated that R0 resection resulted in favorable survival.

The present study revealed that advanced T stage was an unfavorable prognosis factor for overall survival. In fact, it is difficult to identify the T stage when tumors extend to adjacent organs. The positive predictive values of preoperative computed tomographic scans in assessing T4 stage were only 50% [16]. Furthermore, intraoperative assessment of true invasion into adjacent organs may be challenging. Mita et al. reported that 19 of 41 (46.3%) T4 gastric cancer patients had pathologically-confirmed inflammatory adhesions [15]. Similarly, 45% of patients in our study had tumor adhesions to the colon (pT4a) rather than invasion to the colon (pT4b). It is unclear if the involved organs require resection when patients have pT4a (cT4b) gastric cancer. In a previous study, Cheng et al. treated 179 patients with T4 gastric cancer and observed that combined resection achieved a better survival whether or not the tumors are adhere to or invade the adjacent organs [17]. Therefore, extended multi-organ resection is recommended for patients with T4 gastric cancer for curative resection.

Lymph node metastasis is common in T4 gastric cancer. The lymph node metastasis rate in the current study was up to 72.5%. Lymph node metastasis is a commonly reported prognostic factor for poor outcome in patients with T4 gastric cancer. Ozer et al. reported that lymph node metastasis is an independent poor prognostic factor in patients with locally advanced gastric cancer [12]. Jeong et al. revealed that lymph node metastasis (greater than pN3) is an independent poor prognostic factor for patients with T4 gastric carcinoma who underwent curative surgery [18]. Further, it was observed that patients with extensive lymph node metastasis (N2 or N3) had a significantly poorer prognosis compared to patients with limited lymph node metastasis (N0 or N1) [4, 7]. Cheng et al. regarded T4 gastric cancer with N2 or N3 nodal disease as incurable and a contraindication for extensive surgery [17]. In agreement with previous observations, lymph node metastasis, as well as grade of lymph node metastasis, were associated with poorer overall survival in T4 gastric cancer extending to the transverse colon. Taken together with our present results, we recommend performing extended multi-organ resection in T4 gastric cancer patients with limited lymph node metastasis.

Neoadjuvant therapy is increasingly advocated in patients with locally advanced gastric cancer. In the MAGIC randomized trial, 503 patients with gastroesophageal cancer were assigned to perioperative-chemotherapy and surgery ($n = 250$ patients) or surgery ($n = 253$ patients) [19]. In this study, perioperative-chemotherapy and surgery improved overall survival and local control compared with surgery. In the French FFCD 9703 multicenter phase-III trial [20], 224 patients with resectable adenocarcinoma of the lower esophagus, the gastroesophageal junction, or the stomach were randomly assigned to receive surgery and perioperative chemotherapy or surgery alone. Higher R0 resection rates and improved overall survival were achieved in the perioperative chemotherapy group compared with surgery alone group. However, perioperative chemotherapy was not significantly effective for patients with gastric cancer in the multivariate analysis. Another randomized trial (EORTC 40954) including 144 patients with locally advanced adenocarcinoma of the stomach or esophagogastric junction showed that neoadjuvant chemotherapy increased R0 resection rate but failed to improve overall survival compared with surgery alone [21]. The aforementioned studies demonstrate that neoadjuvant chemotherapy can decrease the T and N stage and increase R0 resection rate, whereas a survival benefit from neoadjuvant chemotherapy in distal gastric cancer remain vague. A retrospective analysis from National Cancer Data Base (1998–2011) indicated that neoadjuvant therapy may allow for improved overall survival in patients with T4 gastric cancer [22]. However, only 61.7% (648/1049) of the patients who underwent surgical resection received R0 resection. Also, it was not described whether D2 or D1 lymph node dissections were performed. Thus, RCT studies are required to demonstrate a survival benefit from neoadjuvant therapy in distal gastric cancer.

Conclusion

In conclusion, patients with T4 gastric cancer extending to the transverse colon might benefit from curative resection with acceptable morbidity and mortality, whereas the number of patients in this study was relatively small. Large sample size and randomized controlled studies are required to document the benefits of curative resection in the treatment of T4 gastric cancer extending to the transverse colon.

Abbreviations

TNM Tumor-Node-Metastasis; RCTs:Randomized controlled trials

Declarations

Acknowledgements

None

Disclosures

Drs. Wang, Gao, Wang, Lv, Chen, Nie, Chen, Liu have no conflicts of interest or financial ties to disclose.

Authors' contributions

LY and CX designed this study, collected and analyzed the data, and wrote the manuscript. WG, GC, and WY collected the data and revised the manuscript. LH, CB, and NC collected the data. All authors read and approved the final manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The dataset used and analyzed during the current study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the institutional review board of Affiliated Tumor Hospital of Zhengzhou University. All patient procedures were performed after obtaining written informed consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

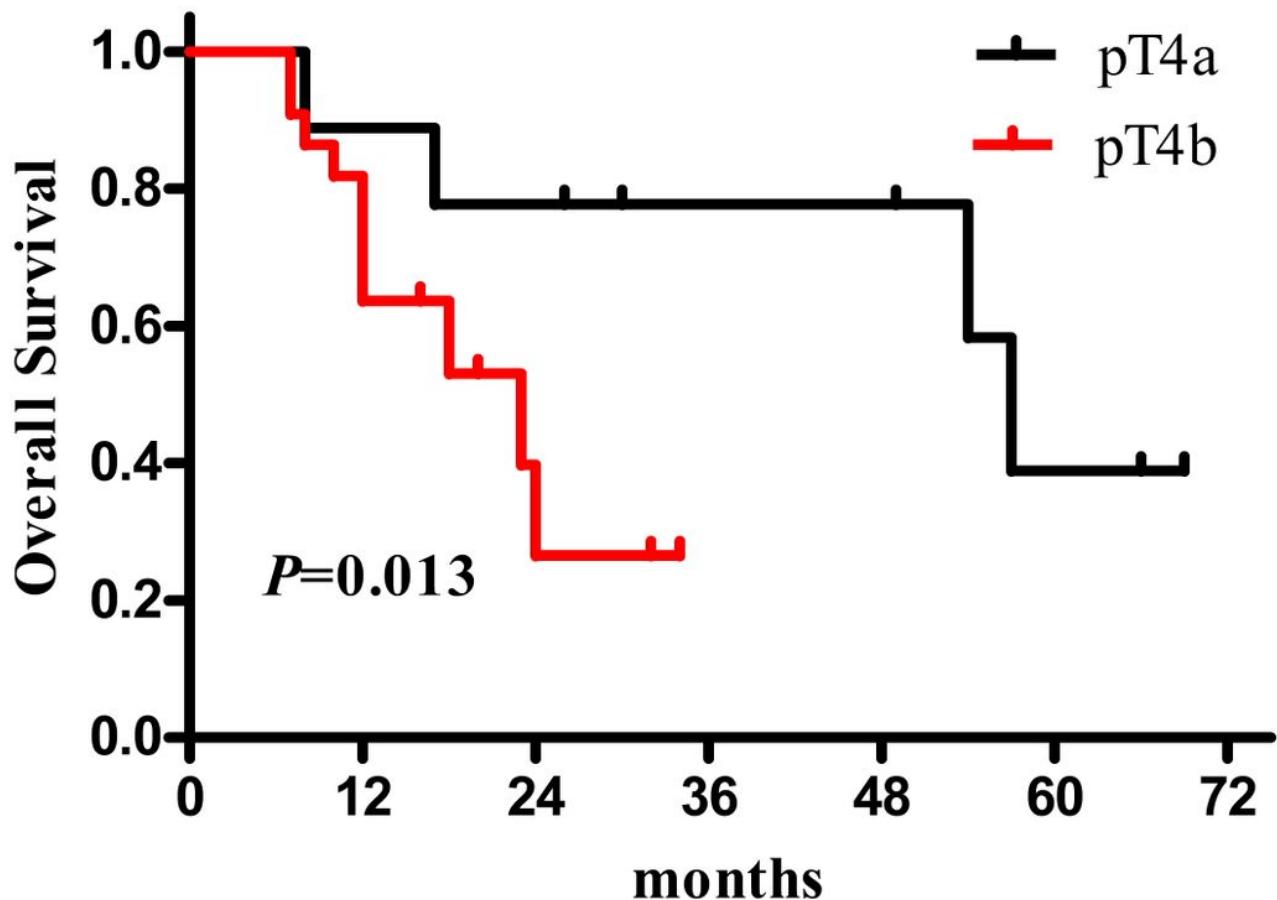


Figure 1

Overall survival on the basis of T stage.

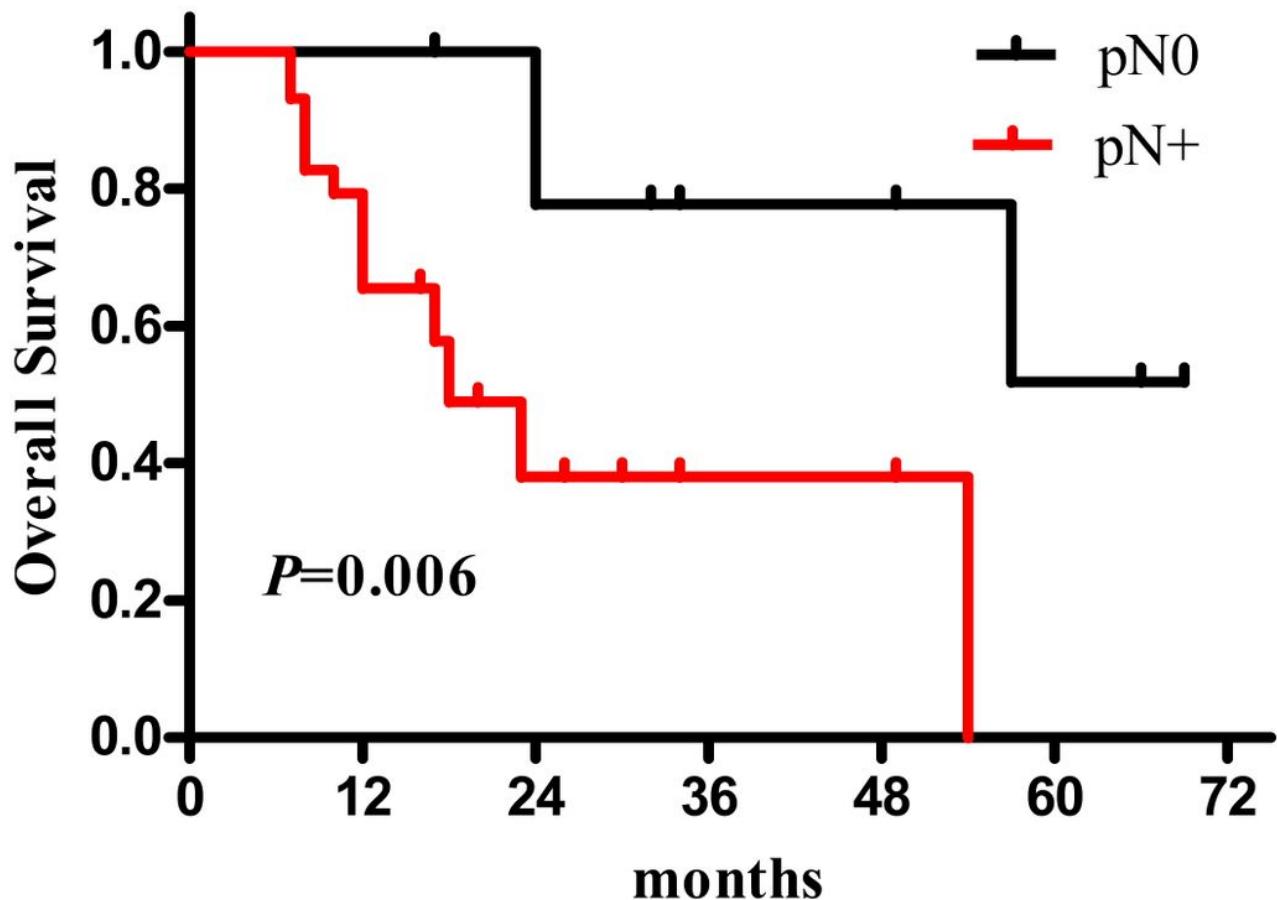


Figure 3

Overall survival on the basis of N stage.

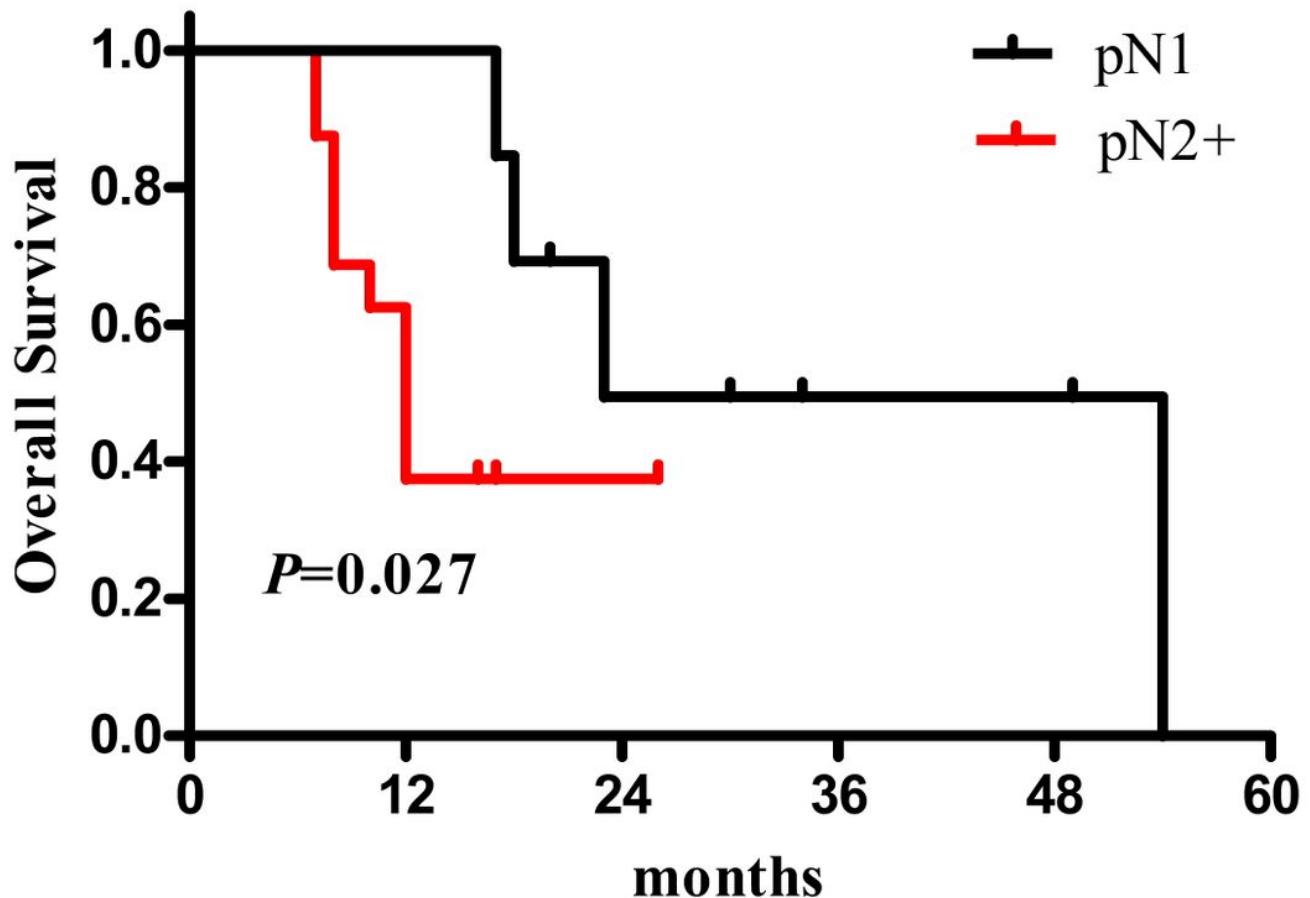


Figure 5

Overall survival on the basis of the extent of lymph node metastasis.