

The role of the metabolic parameters of pre-treatment ^{18}F -FDG PET/CT in patients with locally advanced cervical cancer

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Abstract

Purpose

The purpose of the present study was to evaluate the role of the pre-treatment metabolic parameters of ^{18}F -fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F -FDG PET/CT) in patients with locally advanced cervical cancer (LACC) treated with definitive concurrent chemoradiotherapy (CCRT) or radiotherapy.

Methods

Patients with LACC who underwent pre-treatment ^{18}F -FDG PET/CT examination and definitive CCRT or radiotherapy between February 2010 and December 2015 in our institute were enrolled. For each patient, the maximum standardized uptake value (SUVmax), mean standardized uptake value (SUVmean), metabolic tumour volume (MTV), and total lesion glycolysis (TLG) of the primary tumour were measured. The survival outcomes were calculated with the Kaplan-Meier method. Cox proportional hazards models were used for univariate and multivariate analyses.

Results

A total of 125 patients were finally included in this study. The median follow-up duration was 62 months (range, 4-114 months). The 5-year overall survival (OS), disease-free survival (DFS), local control (LC) and distant metastasis-free survival (DMFS) rates were 83.6%, 75.1%, 92.3% and 79.9%, respectively.

Univariate analysis indicated that $\text{MTV} \geq 18.3 \text{ cm}^3$ showed worse OS and DMFS; however, no significant differences were identified for OS and DMFS in multivariate analyses. $\text{TLG} \geq 113.4$ implied worse DFS and DMFS. In multivariate analysis, $\text{TLG} \geq 113.4$ was an independent predictive factor for OS, DFS and DMFS. SUVmax and SUVmean had no significant influence on OS, DFS, LC or DMFS in either univariate or multivariate analysis.

Conclusion

Pre-treatment $\text{TLG} \geq 113.4$ was associated with a high incidence of disease recurrence and poor OS in patients with LACC.

Introduction

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women worldwide[1]. Cervical cancer ranks eighth in incidence and mortality in China[2]. Almost half of the patients present with locally advanced disease at the time of diagnosis. At present, the primary

treatment approach for patients with LACC is concurrent chemoradiation. In approximately 80% of patients, recurrence of cervical cancer occurs within 2 years after initial treatment. Some prognostic factors have been associated with clinical outcomes, including age, stage, tumour pathology, primary tumour size, lymph node status, squamous cell carcinoma antigen, and human papillomavirus[3–6].

^{18}F -FDG PET/CT has become an essential imaging tool in oncology in addition to conventional radiologic methods such as computed tomography (CT) and magnetic resonance imaging (MRI)[7]. It is widely used in the diagnosis, clinical staging, response evaluation, curative effect observation, failure mode and prognostic analysis of cervical cancer and other tumours[8–12]. In recent years, the association between the metabolic parameters of pre- and post-treatment ^{18}F -FDG PET/CT and treatment failure or survival in cervical cancer has become a research hotspot. Metabolic parameters, such as SUVmax, SUVmean, MTV and TLG, are the focus of attention[13]. On the one hand, some studies have reported the correlations between metabolic parameters and the clinical outcomes of cervical cancer. Patients with cervical cancer with a high SUVmax primary lesion show a worse prognosis[14, 15]. The baseline SUVmean can effectively predict the histopathological partial response of the primary tumour in LACC patients treated with CRT followed by surgery, suggesting the potential role of ^{18}F -FDG PET/CT in personalized treatment[16]. Pre-treatment MTV and TLG are predictors of response to therapy and are associated with OS in cervical cancer patients treated with CRT[17, 18]. On the other hand, there are some dissenting views. The role of SUVmax and SUVmean as prognostic factors for cervical cancer is still controversial[19]. Whether MTV and TLG are important prognostic indicators of cervical cancer remains to be further studied[20].

In this study, we reviewed cervical cancer patients with pre-treatment ^{18}F -FDG PET/CT and analysed the associations between metabolic parameters and treatment failure or survival.

Methods

Patients

We reviewed patients with LACC who underwent a pre-treatment ^{18}F -FDG PET/CT scan and were treated with definitive CCRT or radiotherapy between February 2010 and December 2015 at Peking Union Medical College Hospital. The inclusion criteria were as follows: (1) histologically confirmed cervical cancer; (2) FIGO (2009) stage IB2, IIA2 and IIB-IVA; (3) underwent ^{18}F -FDG PET/CT scan before primary treatment; (4) no evidence of distant metastases; and (5) treated with definitive CCRT or radiotherapy. The exclusion criteria were as follows: (1) underwent conization of the cervix; (2) previous or concurrent diagnosis of secondary primary tumour; (3) Karnofsky performance score <70; and (4) diagnosis of diabetes mellitus.

Pre-treatment evaluations included history, physical, and gynaecological examinations, complete blood count, liver function test, renal function studies, chest and abdomen CT or whole-body PET/CT, and pelvic MRI.

PET/CT technique and image analysis

The imaging agent ^{18}F -FDG, which has both a radiochemical purity and chemical purity greater than 98% and negative 24 h bacterial culture and bacterial endotoxin test by the gel method, was synthesized by the PET centre of Peking Union Medical College Hospital. All patients fasted for at least 4 hours and rested for 90 minutes before an intravenous administration of 3.7-7.4 (0.1-0.2 mCi) MBq/kg body weight ^{18}F -FDG. The blood glucose level was measured before the administration of the radiotracer to ensure that it was less than 8 mmol/l. The PET images were acquired in 3-dimensional mode with a Siemens Biograph 64 PET/CT system from the skull base to the symphysis pubis 1 hour after injection.

The attenuation-corrected volumetric images were displayed in coronal, axial and sagittal views, and they were independently interpreted by 2 experienced PET physicians. The readers reached a consensus in cases of discrepancy. The SUVmax of the primary lesion of the cervix was measured. A contour around the target lesions inside the boundaries was automatically determined, and the region of interest (ROI) with 40% SUVmax of the primary lesion of the cervix within the contouring margin was delineated to define the MTV[20]. The TLG of the primary lesion of the cervix was calculated by multiplying the MTV of the primary lesion of the cervix by its SUVmean.

Treatment

All patients were treated with external beam radiation and high-dose-rate brachytherapy. External beam radiation was delivered with fixed-field intensity-modulated radiation therapy, volumetric-modulated arc therapy, or helical tomotherapy. A total of 50.4 Gy external radiation (1.8 Gy per fraction daily) was delivered to the pelvis, and 59.36-61.6 Gy (2.12-2.2 Gy per fraction daily) was prescribed for the lymph nodes. For patients with para-aortic lymph nodes, the superior border extended to the level of renal vessels or to the upper margin of T12. High-dose-rate brachytherapy was delivered with an Ir-192 source, with 24-36 Gy (biologically effective dose 38.4-57.6 Gy) in four to six fractions to point A. Weekly cisplatin was the first-line recommendation of concurrent chemotherapy. A small number of patients received radical radiotherapy alone.

Follow-up

Patients had follow-up examinations every 3 months in the first 2 years, every 6 months up to 5 years, and then once per year. Recurrence was identified through biopsy or evidence of disease progression on the basis of a series of imaging studies. OS was defined as the time from the start of treatment to death from any cause or the last follow-up. DFS was defined as the time from the end of treatment to recurrence or the last follow-up. LC was defined as the time from the end of treatment to local failure or the last follow-up. DMFS was defined as the time from the end of treatment to distant metastasis or the last follow-up.

Statistical analysis

SPSS software (version 26.0; SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. ROC curve analysis was performed to determine the cut-off values of SUVmax, SUVmean, MTV and TLG that indicated the optimal trade-off by maximizing the sum of sensitivity and specificity for DFS. The Kaplan–Meier method was used to estimate OS, DFS, LC, and DMFS. Univariate and multivariate analyses of the clinical characteristics and metabolic parameters were carried out using the log-rank test and Cox proportional hazards model. To avoid many of the previously significant relationships falling out of the 0.05 significance level, we decided to include variables with $p < 0.1$ in the multivariate analysis, and $p < 0.05$ was considered to be statistically significant.

Results

The detailed characteristics of the enrolled patients are shown in Table 1. According to our inclusion and exclusion criteria, 125 of the 1560 patients were finally included in this study. A total of 112 patients (89.6%) presented with stage IIB or above cervical cancer. A total of 114 patients (91.2%) had squamous cell carcinoma, 9 patients (7.2%) had adenocarcinoma, 1 patient had clear cell carcinoma, and the remaining patient had Mullerian carcinosarcoma. Fifty-two patients (41.6%) had a tumour size greater than 4 cm by gynaecological examination. Forty-three patients (34.4%) had positive pelvic lymph nodes (PLNs) and 2 patients (1.6%) had positive para-aortic lymph nodes (PALNs) confirmed by ^{18}F -FDG PET/CT; 10 patients (8%) with positive PALNs had concomitant PLN metastasis.

Table 1
The characteristics of the enrolled patients

Characteristics	
Total number of patients	125
Age[median(range)](years)	50(30–81)
FIGO(2009) stage	
IB	10 (8%)
IIA	3 (2.4%)
IIB	84 (67.2%)
IIIA	3 (2.4%)
IIIB	24 (19.2%)
IVA	1 (0.8%)
Histology	
Squamous cell carcinoma	114 (91.2%)
Adenocarcinoma	9 (7.2%)
others	2 (1.6%)
Tumour size(cm)	
≤ 4	73 (58.4%)
>4	52 (41.6%)
Pelvic LN involvement	
Para-aortic LN involvement	2 (1.6%)
Both pelvic LN and para-aortic LN involvement	10 (8%)
Overall treatment time(days)	
≤ 56	96 (76.8%)
>56	29 (23.2%)
Total dose of brachytherapy(Gy)	
< 30(fraction range of 5-7Gy)	14 (11.2%)
≥ 30(fraction range of 5-7Gy)	111 (88.8%)
Abbreviations: FIGO = International Federation of Gynecology and Obstetrics; LN = lymph node; SUVmean = mean standardized uptake value; SUVmax = maximum standardized uptake; MTV = metabolic tumor volume; value; TLG = total lesion glycolysis.	

Characteristics	
Number of concurrent chemotherapy(fractions)	
< 4	28 (22.4%)
≥ 4	97 (77.6%)
SUVmean	
< 7.9	74 (59.2%)
≥ 7.9	51 (40.8%)
SUVmax	
< 12.8	68 (54.4%)
≥ 12.8	57 (45.6%)
MTV(cm ³)	
< 18.3	59 (47.2%)
≥ 18.3	66 (52.8%)
TLG	
< 113.4	55 (44%)
≥ 113.4	70 (56%)
Abbreviations: FIGO = International Federation of Gynecology and Obstetrics; LN = lymph node; SUVmean = mean standardized uptake value; SUVmax = maximum standardized uptake; MTV = metabolic tumor volume; value; TLG = total lesion glycolysis.	

All 125 patients completed radiotherapy with a median time of 51 days (range, 42–98 days). Twelve patients (9.6%) received neoadjuvant chemotherapy followed by concurrent chemoradiotherapy or radiotherapy alone, 102 patients (81.6%) received concurrent chemoradiotherapy as the primary therapy, and the remaining 11 patients (8.8%) received radiotherapy alone. Ninety-seven patients (77.6%) completed more than or equal to four cycles of chemotherapy. A total of 111 patients (88.8%) underwent a total dose of brachytherapy greater than or equal to 30 Gy at a single dose range of 5–7 Gy.

The median follow-up period was 62 months (range, 4-114 months). A total of 30 patients (24%) suffered from treatment failure, including 6 patients with local recurrence, 21 patients with distant failure, and 3 patients with concurrent local and distant failure. The total local recurrence and distant failure rates were 7.2% and 19.2%, respectively. The most common site of local recurrence was the cervix uterus, and the most common site of distant metastasis was the lung. The 5-year OS, DFS, LC and DMFS rates were 83.6%, 75.1%, 92.3% and 79.9%, respectively (Fig. 1).

ROC curve analysis was used to determine the best cut-off values of SUVmax, SUVmean, MTV, and TLG in predicting the prognosis of cervical cancer, considering the sensitivity and specificity for DFS. The areas under the curves of SUVmax, SUVmean, MTV, and TLG were 0.53 ($p = 0.595$; 95% CI 0.41–0.65), 0.54 ($p = 0.544$; 95% CI 0.42–0.66), 0.57 ($p = 0.267$; 95% CI 0.45–0.68), and 0.57 ($p = 0.223$; 95% CI 0.46–0.69), respectively. The optimal cut-off points of SUVmax, SUVmean, MTV and TLG were 12.8, 7.9, 18.3 cm³ and 113.4, respectively.

The univariate analysis showed that PALN, total dose of brachytherapy, and TLG were significantly associated with DFS (Table 2). After multivariate analysis, PALN (HR 0.12; 95% CI, 0.05–0.28; $p < 0.001$), total dose of brachytherapy ≥ 30 Gy (HR 3.30; 95% CI, 1.32–8.25; $p = 0.011$), and TLG level ≥ 113.4 (HR 0.28; 95% CI, 0.12–0.64; $p = 0.003$) remained significant in predicting DFS (Table 3). FIGO stage, PALN, total dose of brachytherapy, and TLG were independent prognostic factors for OS in multivariate analysis. PALN was a poor prognostic factor for LC. PALN, total dose of brachytherapy, and TLG had important impacts on DMFS in multivariate analysis. MTV was an important prognostic factor for OS and DMFS in univariate analyses; however, no significant differences were identified for OS and DMFS in multivariate analyses. Moreover, SUVmax and SUVmean had no significant influence on DFS, OS, LC, or DMFS in either univariate or multivariate analysis.

Table 2

Univariate analyses of clinical factors and PET metabolic parameters for disease-free survival

variable	Univariate analysis		
	HR	95%CI	p
Age(continuous, year)	1.003	0.969–1.038	0.882
FIGO(2009) stage			
Ⅱ-Ⅲ vs. Ⅳ-Ⅳ	2.114	0.988–4.523	0.054
Histology			
Squamous vs. non-squamous	2.459	0.939–6.440	0.067
Tumour size(cm)			
≤ 4 vs. >4	1.336	0.651–2.738	0.429
Pelvic LN involvement			
Negative vs. Positive	1.368	0.667–2.805	0.393
Para-aortic LN involvement			
Negative vs. Positive	6.166	2.711–14.024	< 0.001
Overall treatment time(days)			
≤ 56 vs. >56	1.785	0.835–3.818	0.135
Total dose of brachytherapy(Gy)			
< 30 vs. ≥30(fraction range of 5-7Gy)	0.382	0.155–0.942	0.037
Number of concurrent chemotherapy(fractions)			
< 4 vs. ≥4	0.839	0.360–1.956	0.684
SUVmean			
< 7.9 vs. ≥7.9	1.555	0.759–3.187	0.227
SUVmax			
< 12.8 vs. ≥12.8	1.788	0.867–3.688	0.116
MTV(cm ³)			
< 18.3 vs. ≥18.3	2.095	0.980–4.480	0.056
TLG			
Abbreviations: HR = hazard ratio; CI = confidence interval; FIGO = International Federation of Gynecology and Obstetrics; LN = lymph node; SUVmean = mean standardized uptake value; SUVmax = maximum standardized uptake; MTV = metabolic tumor volume; TLG = total lesion glycolysis.			

variable	Univariate analysis		
	HR	95%CI	p
< 113.4 vs. \geq 113.4	2.629	1.169–5.914	0.019
Abbreviations: HR = hazard ratio; CI = confidence interval; FIGO = International Federation of Gynecology and Obstetrics; LN = lymph node; SUVmean = mean standardized uptake value; SUVmax = maximum standardized uptake; MTV = metabolic tumor volume; TLG = total lesion glycolysis.			

Table 3
multivariate analyses of clinical factors and PET metabolic parameters for disease-free survival

variable	multivariate analysis		
	HR	95%CI	p
Para-aortic LN involvement			
Negative vs. Positive	0.116	0.048–0.278	< 0.001
Total dose of brachytherapy(Gy)			
< 30 vs. \geq 30(fraction range of 5-7Gy)	3.296	1.316–8.253	0.011
TLG			
< 113.4 vs. \geq 113.4	0.278	0.121–0.640	0.003
Abbreviations: HR = hazard ratio; CI = confidence interval; LN = lymph node; TLG = total lesion glycolysis.			

The 5-year OS, DFS, LC and DMFS rates for patients with TLG levels < 113.4 and \geq 113.4 were 90.1% and 78% ($p = 0.055$, Fig. 2), 86.5% and 66.1% ($p = 0.015$, Fig. 3), 96.2% and 89.3% ($p = 0.136$, Fig. 4), and 90.9% and 71.2% ($p = 0.02$, Fig. 5), respectively. For the 70 patients with TLG \geq 113.4, the median follow-up period was 61 months (range, 4-110 months). The median DFS period was 56 months. Of these patients, 22 patients (31.4%) experienced treatment failure, including 4 patients with local failure, 15 patients with distant failure, and 3 patients with concurrent local and distant failure. The total local failure and distant failure rates were 10% and 25.7%, respectively. Of the 22 patients who experienced treatment failure, treatment failure occurred within 2 years after treatment in 18 patients (81.8%) and within 5 years after treatment in 22 patients (100%). The 5-year OS, DFS, LC and DMFS rates for patients with MTV levels < 18.3 cm³ and \geq 18.3 cm³ were 90.9% and 76.6% ($p = 0.03$), 83.5% and 67.7% ($p = 0.051$), 94.7% and 90.3% ($p = 0.32$), and 88.4% and 71.8% ($p = 0.031$), respectively.

Discussion

At present, various metabolic parameters of PET, such as MTV and TLG, have particularly become a research hotspot for predicting the prognosis of cervical cancer. However, there are different opinions on the role of PET metabolic parameters in the prognosis of cervical cancer. Some studies have shown that metabolic parameters of PET, such as SUVmax, SUVmean, MTV and TLG, play an important role in

predicting the prognosis of cervical cancer. However, other studies have found no significant correlation between these parameters and survival. Therefore, in our study, we investigated the relationships between clinical characteristics and PET metabolic parameters and the recurrence and long-term survival of cervical cancer. Our study shows that pre-treatment TLG, PALN and total dose of brachytherapy are important independent prognostic factors for recurrence and survival.

SUV can reflect metabolic activity as a semiquantitative marker of tumour uptake and has been demonstrated to play an important role in predicting the prognosis of cervical cancer in previous studies. A meta-analysis demonstrated that a significantly worse prognosis was associated with a higher SUVmax of the primary lesion in cervical cancer. However, SUVmax was not a significant independent prognostic factor in most of the enrolled studies in that meta-analysis[14]. There are various reasons for this contradictory result, especially publication bias, which cannot be ignored. In addition, there are several limitations, such as missing data, the small sample size of each enrolled study and inconsistent treatment methods in different medical centres, which may cause differences in results. Voglimacci et al. also suggested that cervical SUVmax as a continuous variable was a critical predictive index for survival outcomes, but the difference was not statistically significant when using the cut-off value[15]. Fernanda et al. reported that pre-treatment $SUV_{mean} \geq 5$ was a significantly poor prognostic factor of OS (57% vs. 86%, $p = 0.03$), DFS (36% vs. 88%, $p = 0.004$) and LC (65% vs. 88%, $p = 0.04$) in univariate analysis. However, statistically significant associations were not found between SUV_{mean} and survival outcomes in multivariate analysis. Meanwhile, the demonstration of an association between SUVmax and prognosis would have been more challenging to interpret[19]. In our study, SUVmax and SUV_{mean} had no significant influence on OS, DFS, LC or DMFS. There are several articles with similar results to our study[13, 21]. SUV may be affected by many factors, such as body mass index, blood glucose level, scan duration, and reconstruction algorithm[22–24]. Therefore, the role of SUVmax and SUV_{mean} in predicting the prognosis of cervical cancer is still controversial and remains to be further studied.

MTV represents the volume of metabolically active malignant lesions, which is similar but more accurate than the measurement of tumour size on physical examination and may be significantly correlated to the prognosis of the disease. Leseur et al. demonstrated that MTV calculated with a segmentation of 55% SUVmax from pre-treatment PET scans can be used to predict patient survival outcomes after concurrent chemoradiotherapy for LACC[13]. Similarly, Sun et al. also considered that MTV accumulation with a threshold of 40% SUVmax was an important prognostic factor for patients with cervical cancer and should be used to guide oncologists in selecting individualized therapies[25]. Guler et al. took the opposite view that the role of using MTV, defined as the regions equal to or greater than an SUV of 2.5, to predict the prognosis of cervical cancer patients and to change patient treatment management strategies still needs further confirmation[26]. In our study, MTV, calculated with a threshold of 40% SUVmax, presented an obvious association with OS but failed to reach the 0.05 significance level for DFS in univariate analysis; however, there was no significant association between MTV and OS in multivariate analysis. We considered that the reasons for these different results may be related to the inconsistency in the definition of MTV in different studies. Therefore, we believe that MTV alone is not rigorous enough to predict the prognosis of cervical cancer patients in the absence of a consistent definition of MTV.

The combination of MTV and TLG is a more effective prognostic factor that takes into account both metabolic activity and tumour volume as important parameters of tumour response to therapy. Jang Yoo et al. highlighted that TLG (cutoff, 7600), a volume-based metabolic parameter for primary cervical tumours, was a significant predictor of recurrence in cervical cancer in both univariate analysis and multivariate analysis[27]. Likewise, Liang et al. reported that TLG was obviously associated with survival outcomes in patients with locally advanced cervical cancer[28]. Similarly, Carpenter et al. indicated that TLG measured by ¹⁸F-FDG PET/CT was associated with OS in patients with high-risk cervical cancer treated with chemoradiotherapy and brachytherapy[18]. Lima et al. also preliminary suggested that although its p value seems to be below the critical value, pre-treatment TLG was a significant independent predictor of response to therapy[17]. However, the sample sizes of these studies were less than 100 cases. In our group, we obtained similar results and had a larger sample size. Although TLG confronts the same challenges as MTV, we still believe that the combination of multiple parameters makes predictions more effective.

In our study, we found that distant metastasis in patients with LACC treated with chemoradiotherapy and brachytherapy was a major pattern of treatment failure. This finding was consistent with that of previous research. Importantly, we found that TLG was a significant independent prognostic factor for DMFS and OS. The role of adjuvant chemotherapy followed by chemoradiotherapy is still controversial. Dueñas-González et al. investigated 515 patients with locally controlled cervical cancer in a randomized study[29]. The results showed that the 3-year PFS of concurrent chemoradiotherapy following two adjuvant cycles of cisplatin plus gemcitabine was significantly improved compared with standard treatment (74.4% vs 65.0%, $p = 0.029$); the same result was found for OS (log-rank $p = 0.0224$; HR, 0.68; 95% CI, 0.49 to 0.95). However, the intervention group had more grade 3 and 4 toxicities than the control group ($p < 0.001$). Adjuvant chemotherapy has not been widely accepted because further studies are needed to demonstrate the contributions of multiagent chemoradiotherapy and adjuvant chemotherapy to survival outcomes, and toxicity cannot be ignored.

Local recurrence in cervical cancer patients treated with definitive CCRT or radiotherapy was another pattern of treatment failure. MRI-guided adaptive brachytherapy, which plays an important role, increased the radiation dose to the tumour and led to a significant improvement in the LCR while minimizing the radiation dose delivered to surrounding normal tissues[30, 31]. In our study, we also found that for the 22 patients with $TLG \geq 113.4$ who experienced treatment failure, disease recurrence occurred in all patients within 5 years after treatment. Thus, active follow-up for at least 5 years is essential. These findings may provide an early signal-individualized intensive treatment approach with either adjuvant chemotherapy or MRI-guided adaptive brachytherapy.

The present study demonstrated the role of the metabolic parameters of pre-treatment ¹⁸F-FDG PET/CT as prognostic factors in patients with LACC; however, our study also had several limitations, including the small number of patients included, the retrospective nature and the heterogeneity of the treatment methods. Further prospective studies with larger numbers of patients are needed to confirm these results.

Conclusion

We showed that $TLG \geq 113.4$ of the primary cervical tumour was associated with an increased risk of recurrence and poor overall survival in patients with locally advanced cervical cancer who underwent definitive CCRT or radiotherapy. Patients with high TLG may benefit from intensive therapeutic methods and a longer follow-up duration.

Abbreviations

^{18}F -FDG PET/CT = ^{18}F -fluorodeoxyglucose positron emission tomography-computed tomography; LACC = locally advanced cervical cancer; CCRT = concurrent chemoradiotherapy; SUVmax = maximum standardized uptake value; SUVmean = mean standardized uptake value; MTV = metabolic tumour volume; TLG = total lesion glycolysis; OS = overall survival; DFS = disease-free survival; LC = local control; DMFS = distant metastasis-free survival; CT = computed tomography; MRI = magnetic resonance imaging; PLNs = positive pelvic lymph nodes ; PALNs = para-aortic lymph nodes; FIGO = International Federation of Gynecology and Obstetrics; HR = hazard ratio; CI = confidence interval.

Declarations

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding authors on

reasonable request.

Authors' contributions

Dunhuang Wang was responsible for statistical analysis and drafted the manuscript; Fuquan Zhang and Ke Hu participated in the conception and the design of the study and revised the manuscript; Weiping Wang, Li Huo, Qingqing Pan, Xue Ren performed data collection and interpretation. All authors read and approved the manuscript.

Ethics approval and consent to participate

The study accords with principle of ethics. The Institutional Review Board of Peking Union Medical College Hospital reviewed and approved the protocol.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflicts of interest.

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Figures

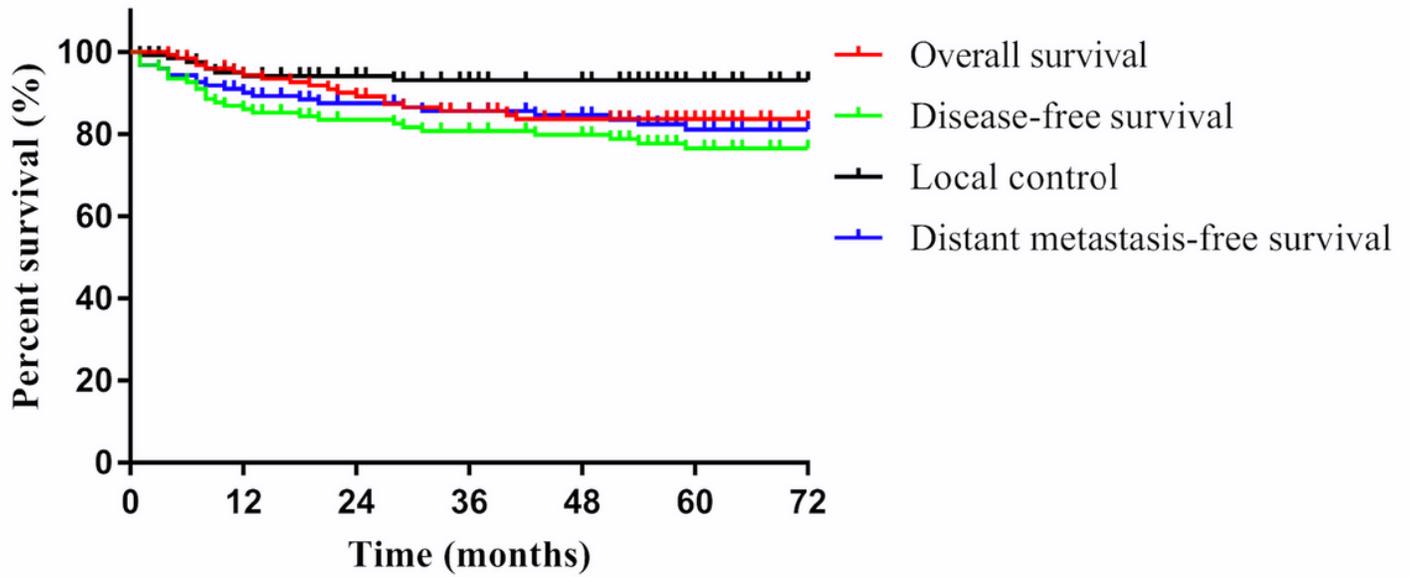


Figure 1

The 5-year overall survival, local control, disease-free survival, and distant metastasis-free survival curves of the enrolled patients.

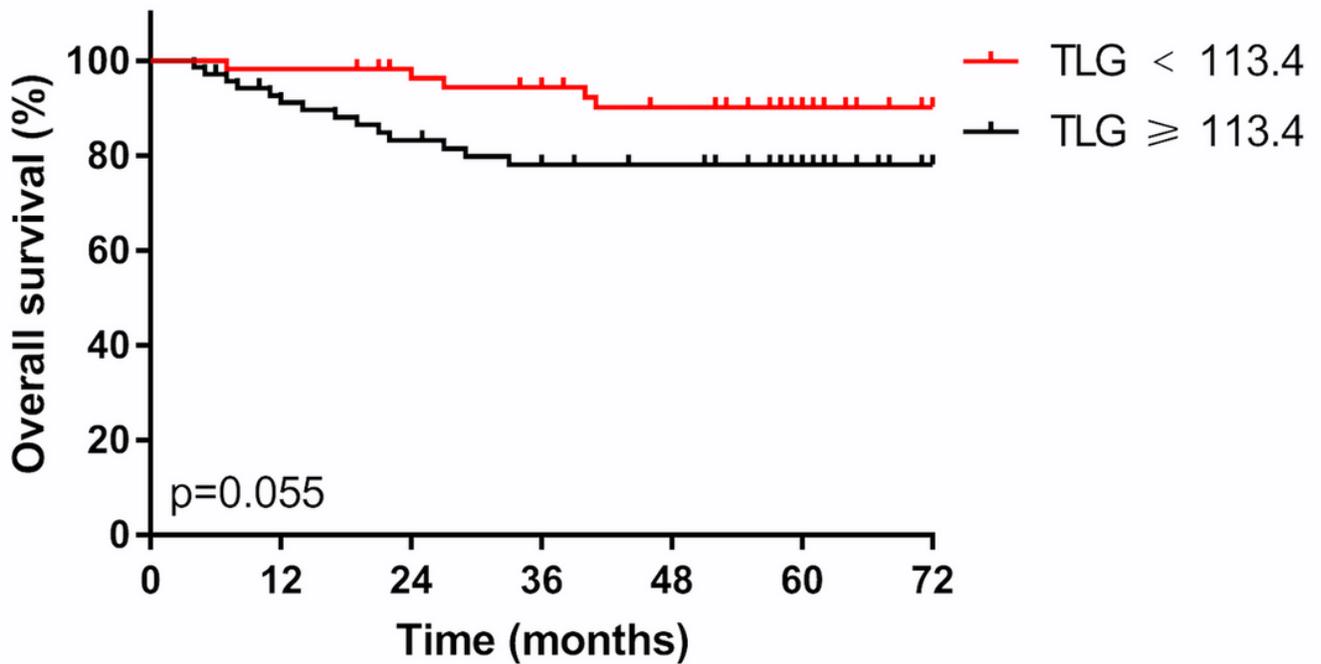


Figure 2

Kaplan-Meier curves of overall survival for TLG (p = 0.055). Abbreviations: TLG = total lesion glycolysis.

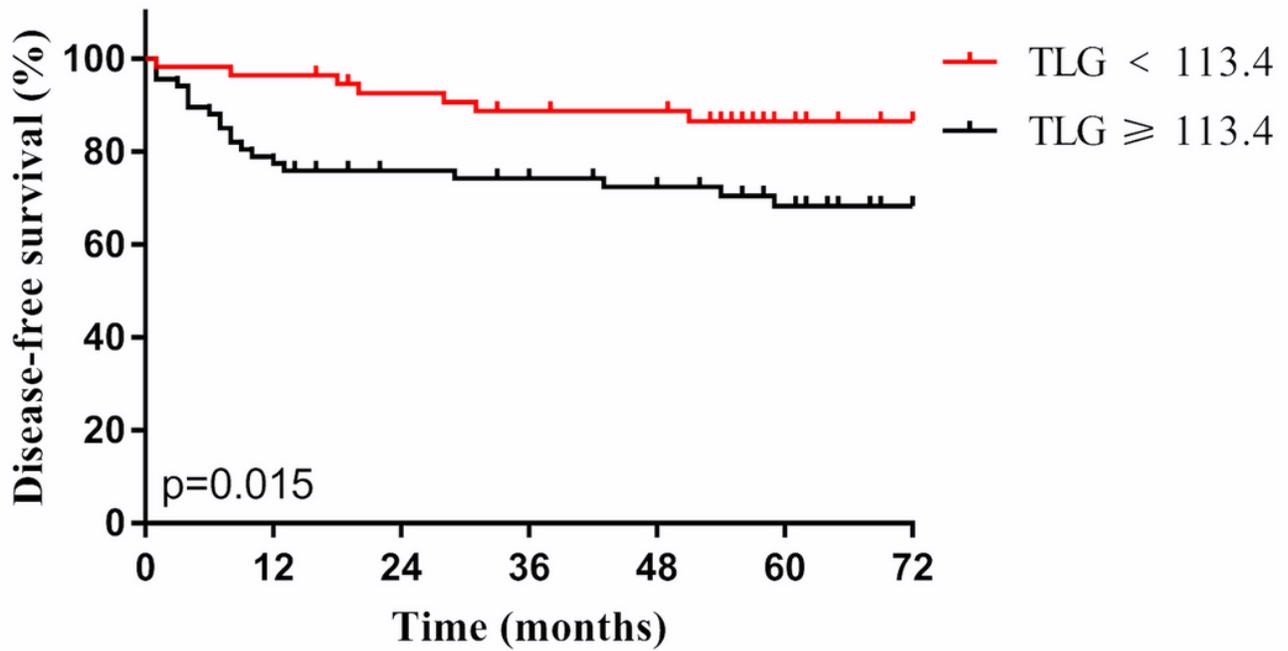


Figure 3

Kaplan-Meier curves of disease-free survival for TLG. Patients with TLG ≥ 113.4 showed worse disease-free survival (p = 0.015). Abbreviations: TLG = total lesion glycolysis.

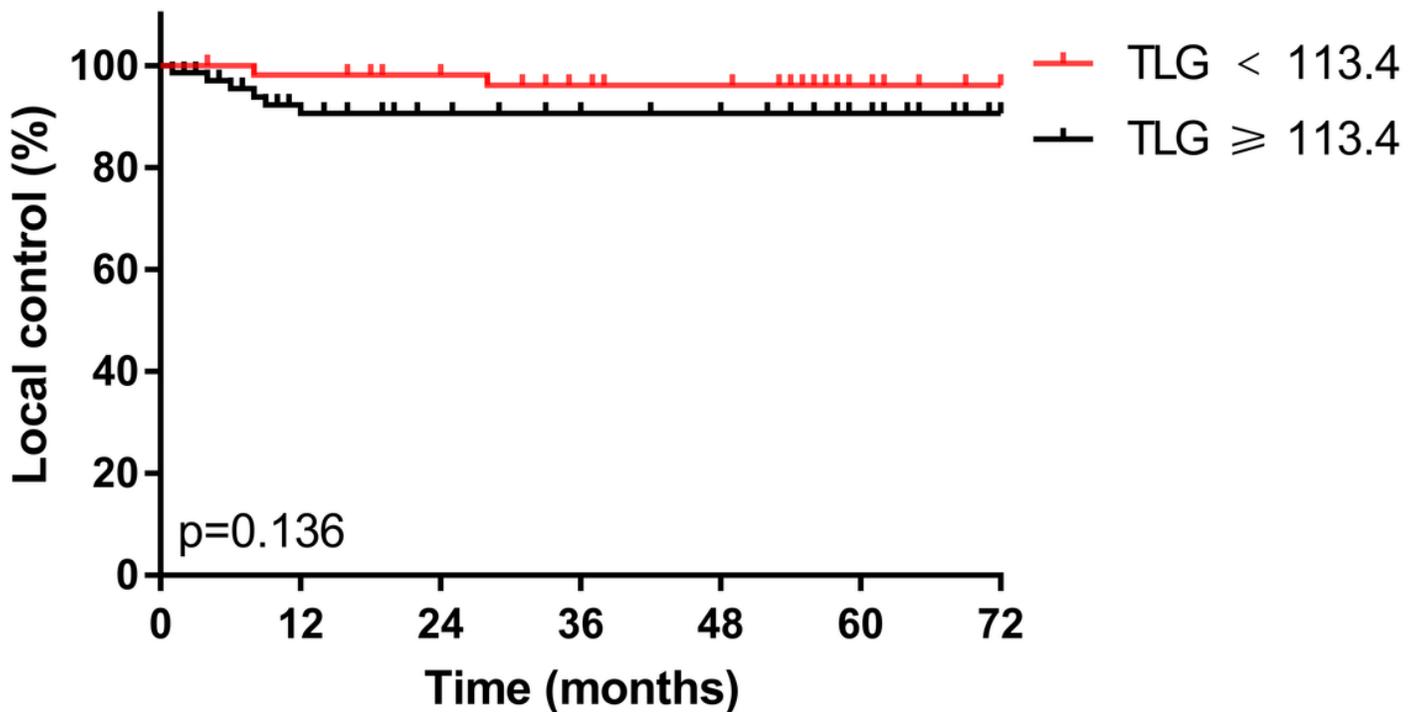


Figure 4

Kaplan-Meier curves of local control for TLG ($p = 0.136$). Abbreviations: TLG = total lesion glycolysis.

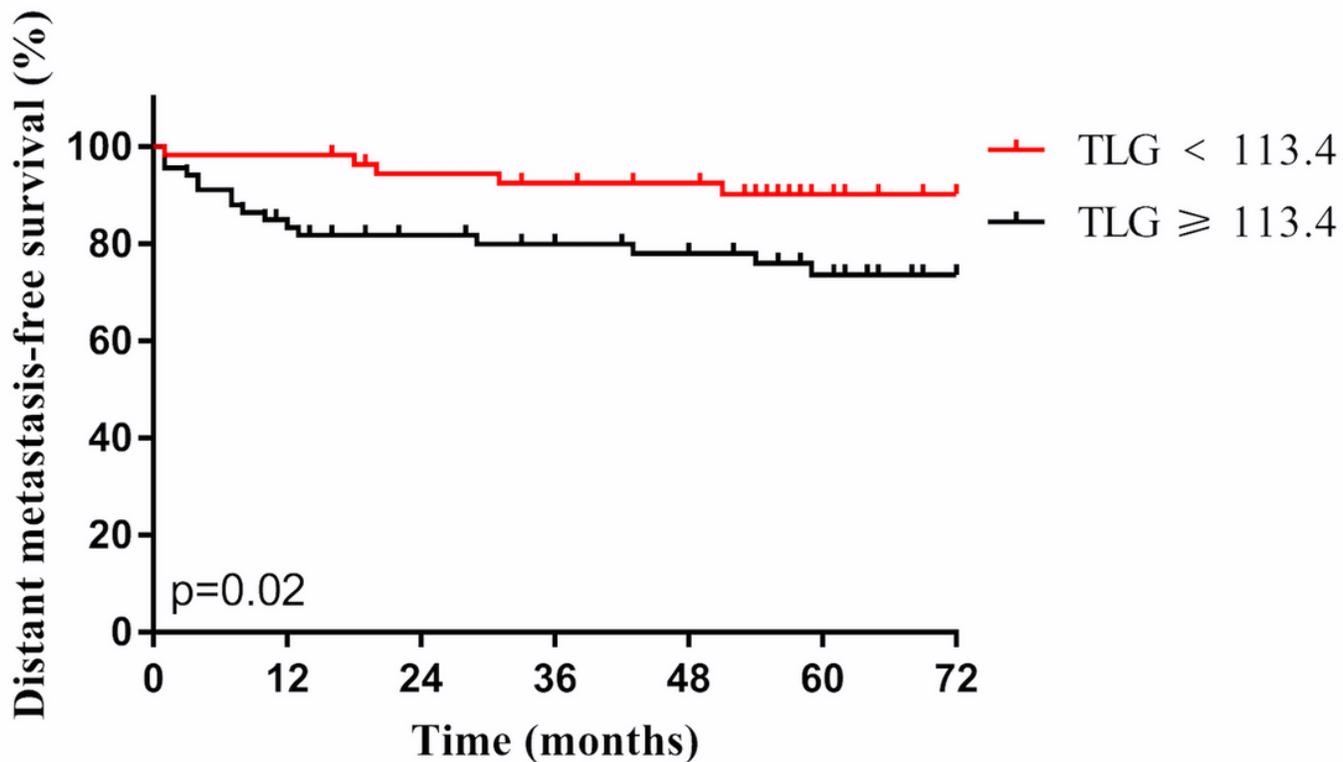


Figure 5

Kaplan-Meier curves of distant metastasis-free survival for TLG. Patients with TLG ≥ 113.4 showed worse distant metastasis-free survival ($p = 0.02$). Abbreviations: TLG = total lesion glycolysis.