Systematic Review and Meta-Analysis

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Prognostic value of maximum standard uptake value, metabolic tumor volume, and total lesion glycolysis of positron emission tomography/computed tomography in patients with nasopharyngeal carcinoma

A systematic review and meta-analysis

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Abstract

Background: The maximal standard uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of positron emission tomography/computed tomography (PET/CT) in patients with nasopharyngeal carcinoma (NPC) perform as new prognostic factors, but the outcomes of the published articles were inconclusive. In this meta-analysis, we evaluated the prognostic value of SUVmax, MTV, and TLG of PET/CT in patients with NPC.

Methods: Relevant English articles were searched in PubMed and EMBASE. The data of patients and the survival outcomes were extracted. Pooled hazard ratios (HRs) were accounted to assess the prognostic value of the SUVmax, MTV, and TLG.

Results: This meta-analysis combined 10 primary studies including 941 patients with NPC. The combined HRs (95% confidence interval [CI] of higher SUVmax, higher MTV, and higher TLG for event-free survival were 2.33 (95% CI, 1.39–3.91, $P = .001$), 2.51 (95% CI, 1.61–3.91, $P < .0001$), and 2.74 (95% CI, 1.91–3.93, $P < .00001$), respectively. Regarding overall survival, the combined HRs were 2.50 (95%CI, 1.65–3.78, $P < .0001$) with higher SUVmax, 3.30 (95% CI, 1.92–5.69, $P < .0001$) with higher MTV and 3.18 (95% CI, 1.70–5.96, $P = .0003$) with higher TLG.

Conclusion: SUVmax, MTV, and TLG were significant prognostic predictors in patients with NPC. And the results suggested that higher SUVmax, MTV, and TLG were associated with worse prognosis.

Abbreviations: CI = confidence interval, DFS = disease-free survival, DMFS = distant metastasis-free survival, EFS = event-free survival, HR = hazard ratio, MTV = metabolic tumor volume, NPC = nasopharyngeal carcinoma, OS = overall survival, PET = positron emission tomography, PFS = progression-free survival, SUVmax = maximum standard uptake value, TLG = total lesion glycolysis.

Keywords: MTV, nasopharyngeal carcinoma, prognosis, SUVmax, TLG

1. Introduction

Nasopharyngeal carcinoma (NPC) is a common malignant tumor in Asia, which occurs in 20 to 30 per 100,000 people per year.[1,2] However in western countries, it is an unusual form of squamous cell carcinoma.[3] Nowadays, it is widely convinced that biopsy of the primary site or fine needle aspiration (FNA) of the neck can be used in diagnosing NPC eventually.[4] Radiotherapy (RT) is the primary treatment of NPC. Intensity-modulated radiotherapy (IMRT) is a new method that provides high radiation doses to the target with less harm to adjacent organs.[5] The increase of dose with IMRT could decrease recurrence and relapse.[6] NPC patients in stage T1N0M0 can be treated by RT only[7] without chemotherapy, but T3-T4 stage patients have a control rate of 30% to 60% if they undergo RT only.[8–10] The control rate will increase after treated with the combination of RT and concurrent platinum-based chemotherapy. In recent studies, the expression of p53 and epidermal growth factor receptor (EGFR) was researched in NPC, and the article analyzed the relation between their expression and survival.[11] In addition, Epstein-Barr virus DNA level was also recommended as a new factor in the prognosis of NPC.[12] But these prognosis factors cannot reflect the tumor burden and tumor aggressiveness in NPC. Fludeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is recommended to find the metastasis after diagnosed.[13] Fluorine-18 fludeoxyglucose (18F-FDG) reflecting glucose metabolism is used in positron emission tomography

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QL, JZ, and WC contributed equally to this study.

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(PET) and in particular integrated PET/CT, which are widely used techniques in the cancer staging assessment in recent years.[13] Staging system is a considered factor to predict prognosis by American Joint Committee on Cancer (AJCC).[14] The maximal standard uptake value (SUVmax) is used to quantify the lesion's metabolism.[15] And it is a recommended factor to predict the prognosis of the primary tumor in some studies. There are some opposite options that the SUVmax provide a threshold defining the tumor,[16,17] but it does not account other aspects of the tumor.[18] Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) calculated by multiplying MTV by mean SUV were considered as prognosis values besides SUVmax.[19] TLG can describe the stereoaggressiveness of tumor. They can be measured efficiently by the available commercial tools. One study reported the prognostic value of MTV and TLG in head and neck cancer (HNC) in 2014[20] and they also reported the prognosis value of volumetric parameters of 18F-FDG PET in non-small-cell lung cancer in 2015.[21] And NPC is a kind of HNC. However, some articles reported different results. The article reported that high SUVmax was a positive factor of DFS in 2015.[22] According to the study by Xie et al, SUVmax and MTV are suggested as significant prognostic markers for PFS in diffuse large B cell lymphoma.[23] Therefore, we designed a meta-analysis to work out the prognosis value of SUVmax, MTV, and TLG in NPC.

2. Methods

2.1. Search strategy and study selection

As this is a meta-analysis, ethical approval was not necessary. A comprehensive literature search of PubMed and EMBASE was performed to find out relevant English articles about volumetric parameters in the prognosis in NPC. The retrieved articles were searched by the combination of the following keywords: (nasopharyngeal carcinoma OR nasopharynx cancer) AND PET/CT AND (prognosis OR prognostic). References of selected studies were also screened for additional relevant studies. Two independent researchers screened the articles respectively making sure that every article was scrutinized. Any discrepancy was solved by consensus.

Only the relevant articles were included and the inclusion criteria in the meta-analysis were as follows: articles are reported in English original high-quality magazines, each has at least 20 patients, 18F-FDG PET/CT scans before treatment, one cutoff data was reported at least, the studies investigated the relationship between the volumetric parameters of 18F-FDG PET/CT and the prognosis of patients. Studies were eliminated based on any of the following conditions: review, case reports, laboratory articles, and letters; analyzed in diverse tumors but with no specific results of NPC; lacked important information for analysis with methods developed by Parmar et al[24] (1998), Williamson et al[25] (2002), and Tierney et al[26] (2007); non-English articles.

2.2. Data extraction

Extracted data concluded the following: author, publication time, sample number; patient characteristics, that is, patients' age, their sex, histology, TNM staging; the result measures median and cutoff values of SUVmax, MTV, and TLG, prognosis-free survival (PFS), disease-free survival (DFS), overall survival (OS), distant metastasis-free survival (DMFS); hazard ratios (HRs) and their 95% confidence intervals (CIs), *P* values of the log-rank test and the Kaplan–Meier survival curve; raw data to calculate HR and standard error (SE) for the patients with high parameters comparing to low parameters.

2.3. Data analysis

We conformed to the similar methodology, which was used in previous study. DFS and PFS were got as primary outcomes and were defined as event-free survival (EFS), which was measured from the date of initiation of therapy.[27] To compare the prognosis, logHR and SE were statistically combined, but the essential data were not always explicit. For this reason, we calculated the data based on Parmar et al[24] (1998), Williamson et al[25] (2002), and Tierney et al[26] (2007). The logHR and SE can be calculated if any following data were given: the HR and 95% CIs, the *P* value for the log rank or Mantel-Haenszel test, and the Kaplan–Meier survival curves. We carried out the meta-analysis in subgroup, categorized by tumor stage, sex, and the delineation of tumor. Figure was carried through by the software contrived by Matthew Sydes and Jayne Tierney with these methods on survival.[26] Positive group means that the value of volumetric parameters patients in this group is higher. We considered HR as the effect factor of the study. HR >1 points that positive group had worse outcome compared to negative group under the circumstance that the 95% CIs did not overlap 1. The heterogeneity of the studies was measured by *P* values and I^2. Heterogeneity was significant with $P < .10$ or $I^2 > 50\%$[28] (Higgins et al, 2003).When heterogeneity was acceptable ($P \geq .10$, $I^2 \leq 50\%$), a fixed-effect model was used for next step. Begg test was used to measure publication bias ($P < .05$ indicates statistically significant). RevMan 5.1 (Cochrane collaboration, Oxford, UK) was applied in the study to calculate the data.

3. Results

3.1. Study selection and characteristics

Using the search strategy defined before, 66 articles were found. After screening the titles and abstracts, 30 articles were further screened. One was a case report. Eight articles were reviews and 10 articles were excluded after screening full text. One article was excluded because of incomplete data. Ten studies[14,15,22,29–35] published from 2010 to 2015 were enrolled in the research. The details of the selection were presented in the Figure 1.

The study characteristics were shown in Table 1. Three of the involved articles were prospective, and the others were retrospective. Seventy-three percent of the whole 941 patients were males. The average age of all was 50.22 years. There was no significant difference in the sex and age among the studies. The number of patients in the studies ranged from 40 to 196. Ten articles measured SUVmax, 6 measured MTV, 5 measured TLG, and only 4 articles measured all of them. The cutoff value of SUVmax ranged from 7.8 to 18, MTV ranged from 12.71 to 110, and TLG ranged from 55.01 to 7640. People were divided into 2 groups, lower volume group and higher volume group, based on the cutoff parameters.

Most of the articles included primary NPC, whereas 3 articles reported advanced NPC, 1 reported recurrence, and 1 reported metastatic NPC. Most articles reported outcomes that high SUVmax was a negative prognostic factor, and only 1 reported that high SUVmax led to positive prognosis. All the articles showed that pretreatment high value of MTV and TLG led to negative prognosis.

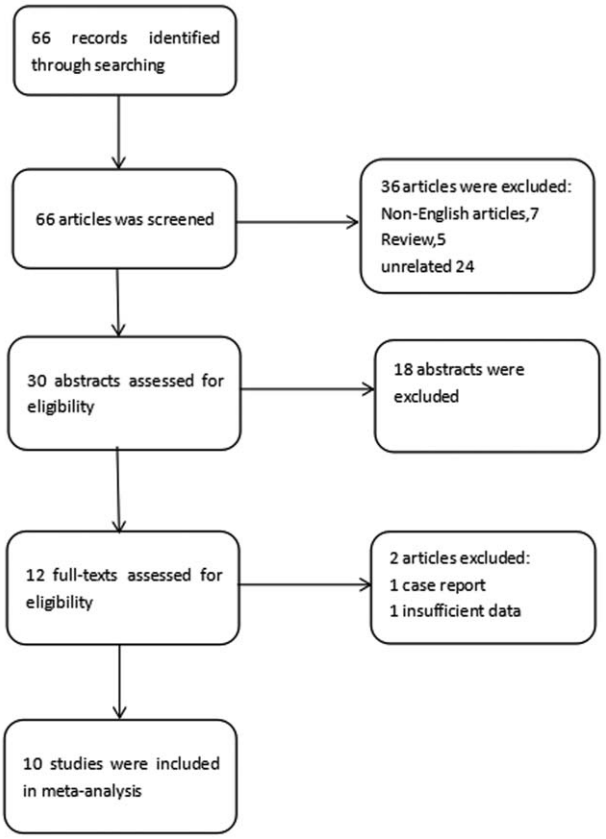

Figure 1. Selection process of studies.

3.2. Primary outcome: EFS

Five articles about SUVmax were included in the research. Based on the cutoff value, the patients were divided into 2 groups, the higher and the lower. The combined HR for EFS of higher SUVmax was 2.33 (95% CI, 1.39–3.91, $P=.001$) (Fig. 2). There was no significant heterogeneity between the articles ($I^2=0\%$, $P=.48$). We performed subgroup analyses base on the delimiting of volume of interest (VOI). The HR was 2.29 (95% CI, 1.36–3.84; $P=.002$) for a higher SUVmax delimited by the tumor and lymph node (LN) (Fig. 3) and there was only 1 article delimiting by the tumor. Another subgroup analysis was performed based on tumor recurrence or metastasis. Among studies including SUVmax, those with primary carcinoma had an HR of 3.11 (95% CI, 1.30–7.44, $P=.01$), and those with locally advanced carcinoma had an HR of 1.99 (95% CI, 1.04–3.78, $P=.04$).

Four articles about MTV were included in the research. The combined HR for EFS of higher MTV was 2.51 (95% CI, 1.61–3.91, $P<.0001$) (Fig. 2). There was no significant heterogeneity between the articles ($I^2=0\%$, $P=.47$). We performed subgroup analyses based on the delimiting of VOI. The HR was 1.44 (95% CI, 0.59–3.50; $P=.42$) (Fig. 4) for an MTV delimited by the tumor and LN and the HR was 3.02 (95% CI, 1.81–5.02; $P<.0001$) for an MTV delimited by the tumor. Another subgroup analysis was performed based on tumor recurrence or metastasis. Among studies containing MTV, those with primary tumor had an HR of 2.74 (95% CI, 1.26–5.95, $P=.01$), and those with metastasis carcinoma had an HR of 2.41 (95% CI, 1.41–4.13, $P=.001$).

Five articles about TLG were included in the research. The combined HR for EFS of higher TLG was 2.74 (95% CI, 1.91–3.93, $P<.00001$) (Fig. 2). There was no significant heterogeneity between the articles ($I^2=36\%$, $P=.18$). The subgroup analysis was performed based on tumor recurrence or metastasis. Among studies containing TLG, those with primary tumor had an HR of 3.41 (95% CI, 2.09–5.57, $P<.00001$) (Fig. 5), and those with metastasis carcinoma had an HR of 2.10 (95% CI, 1.23–3.60, $P=.007$).

DMFS was an important parameter in predicting prognosis. It was an event occurring after the EFS and the distant metastasis was an important factor in predicting prognosis. The HR for DMFS of higher SUVmax was 2.81 (95%CI, 1.54–5.13, $P=.008$), for MTV the HR was 5.42 (95%CI, 1.27–23.11, $P=.02$) and for TLG the HR was the same as MTV.

3.3. Secondary outcome: OS

Six articles involving SUVmax were contained in the analysis. The combined HR for the overall survival of higher SUVmax was 2.50 (95% CI, 1.65–3.78, $P<.0001$) (Fig. 6). VOI was used to define the subgroup analysis. The HR of higher SUVmax defined by the tumor and lymph node was 2.56 (95% CI, 1.32–4.95, $P=.005$) (Fig. 7) and for the tumor group was 2.45 (95% CI, 1.44–4.20, $P=.001$). Another subgroup analysis was performed

Table 1

Characteristics of the included studies.

Study	Year	Country	Study design	No. of patients	Age	Male (%)	Tumor	Staging	Treatment	Endpoingts	Follow-up	Parameters	VOL	Tumor delineation	SUV max-T	MTV (cm3)-T	TLG-T
Yang et al[22]	2015	China	R	40	52.5	72.5	LANC	T3–4N0–3	CT + RT/CCRT + IMRT	LC/PFS/OS	30.5 (24.0–68.0)	SUVmean/SUVmax/ MTV/TLG	T + LN	SUV 2.5	15.6	28.9	249.1
Xiao et al[33]	2015	China	P	179	43	79.9	Primary	stageI-IV	IMRT ± CT	DMFS/OS	84.5 (6–118)	SUVmax	T		10.22		
Yoon et al[35]	2014	Korea	R	40	48	75	Primary	stageI-IV	RT ± CT	OS	32.5 (27.2–59.8)	SUVmax/MTV	T	SUV 2.5/3.0	8.9	31.45/23.01	
Moon et al[30]	2015	Korea	R	44	51	81.8	Primary	stageII-IVB	CCRT + CT	DFS	34.7 (9.0–71.6)	SUVmean/SUV max/MTV/TLG	T	MBP as a threshold	7.8	66	7640
Shi et al[14]	2014	China	R	43	45	74.4	Primary	stage I-IV	CCRT/CT + RT	DMFS/PFS/OS	32 (23–68)	SUVmean/SUVmax/ MTV/TLG	T + LN	SUV 2.5	8.69	12.7	58.08
Shen et al[31]	2015	China	R	194	49	80.4	Recurrence	stage I-IV	RT ± CCRT; CT ± CCRT	OS/LC	18.09 (0.62–55.88)	SUVmax	T		8.65		
Chan et al[32]	2013	Taiwan, China	P	56	55	82.1	Metastasis	IV stage (56)	CT ± RT	PFS/OS	32.6 (20–54)	SUV/MTV/TLG	T	SUV 2.5	12	110	560
Chan et al[29]	2011	Taiwan, China	P	196	48	67.9	Primary	stage III-Ivb	RT ± CT	FFS/DFS/OS	53 (2–97)	SUVmax/MTV/TLG	T + LN	SUV 2.5	18	45	330
Xie et al[34]	2010	China	R	62	43	75.8	LANC	stageIII-IVa-b	CCRT ± CT	DFS/OS	61 (9–69)	SUVmax	T + LN	SUV 2.5	8		
Chan et al[15]	2010	China	R	46	48	76	Primary	stage I-IV,	CCRT/RT ± CT	DFS	13.6 (6.8–29.9)	SUVmax	T + LN	SUV 2.5	7.5		

CCRT = concurrent chemoradiation, CT = chemotherapy, DFS = disease-free survival, DMFS = distant metastasis-free survival, IMRT = intensity-modulated radiotherapy, LANC = locally advanced nasopharyngeal carcinoma, LC = local control, LN = lymph node, MBP = mediastinal blood pool, MTV = metabolic tumor volume, OS = overall survival, PFS = progression-free survival, RT = radiotherapy, SUVmax = maximum standard uptake value, T = Tumor, TLG = total lesion glycolysis.

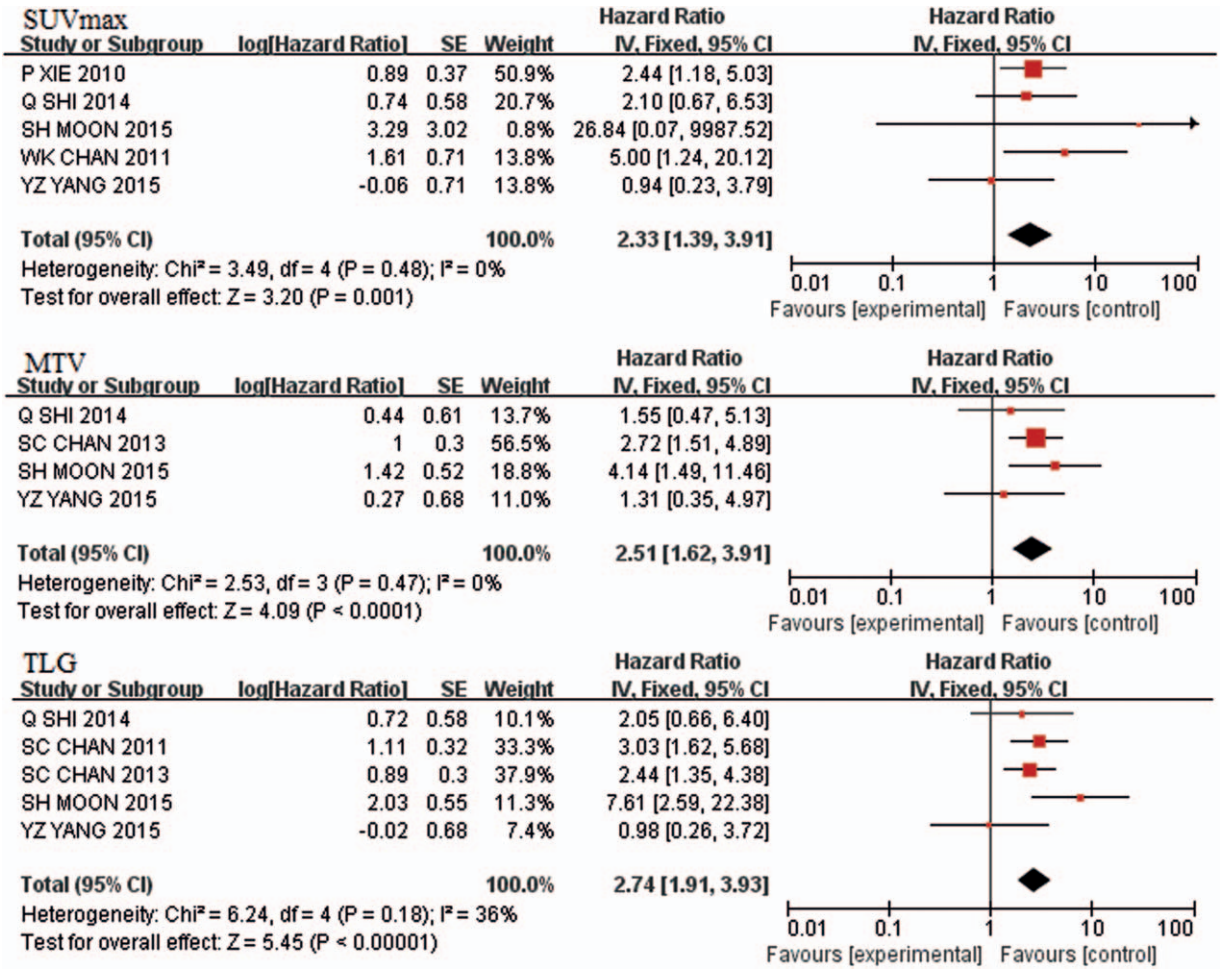

Figure 2. Forest plots of hazard ratio of event-free survival of SUVmax, MTV, TLG. CI = confidence interval, MTV = metabolic tumor volume, SUVmax = maximum standard uptake value, TLG = total lesion glycolysis

based on tumor recurrence or metastasis. Among studies including SUVmax, those with primary carcinoma had an HR of 2.32 (95% CI, 1.35–3.99, $P = .002$), and those with recurrence or metastasis had an HR of 2.77 (95% CI, 1.44–5.33, $P = .002$). The combined HR for OS of higher MTV was 3.30 (95%CI, 1.92–5.69, $P < .0001$) (Fig. 6). We performed subgroup analyses based on the delimiting of VOI. The HR was 3.09 (95% CI, 0.84–11.37, $P = .09$) for a higher MTV delimited by the tumor and LN and the HR was 3.35 (95%CI, 1.84–6.09, $P < 0.0001$) for a higher MTV delimited by the tumor. Another subgroup analysis was performed based on tumor recurrence or metastasis. Among studies including MTV, those with primary carcinoma had an HR of 4.30 (95% CI, 1.48–12.48, $P = .007$), and those with metastasis had an HR of 3.01 (95% CI, 1.60–5.66, $P = .0006$) (Fig. 8). The combined HR of higher TLG was 3.18 (95% CI, 1.70–5.96, $P = .0003$). All the articles were delimited by tumor and lymph node, so no subgroup analysis was performed.

4. Discussion

Staging assessment has been convinced as a prognostic factor of the malignancy.[36] So it is important to distinct the stage of tumor in prognosis. Volumetric parameters of PET/CT such as SUVmax, MTV, and TLG are widely convinced that they can help staging the tumor.[37] So if the value of the volumetric parameters can contribute to predict metastasis and survival, the patients may benefit from it. One study found out that the SUV of 18-FDG PET/CT is a helpful tool to predict the EFS and OS in colorectal cancinoma patients with liver metastases.[38] Another study reported that higher values of SUVmax, MTV, or TLG forecasted a higher risk of recurrence or death in non-small cell lung cancer patients who received surgery.[39] Several published original studies aimed at finding the prognostic value of SUVmax, MTV, and TLG for NPC. Our meta-analysis is the first article to report the prognostic value of SUVmax, MTV, and TLG in NPC. Ten published studies were included to accumulate the evidence on the connection between the prognosis of the volumes of SUVmax, MTV, and TLG in NPC in our meta-analysis. The results showed that SUVmax, MTV and TLG can be used to predict the prognosis of the EFS and OS in NPC patients.

Although MTV or TLG may be affected by variable reasons, our results indicated that high volumetric parameters of PET had worse prognostic value in EFS or OS. In our meta-analysis, the results revealed that higher SUVmax reflected negative prognostic value, with apparent poorer combined HRs for EFS and OS: 2.33 (95% CI, 1.39–3.91, $P = .001$) and 2.50 (95% CI, 1.65–3.78, $P < .0001$), respectively. It also showed that higher TLG and MTV reflected negative prognostic value. One study[20]

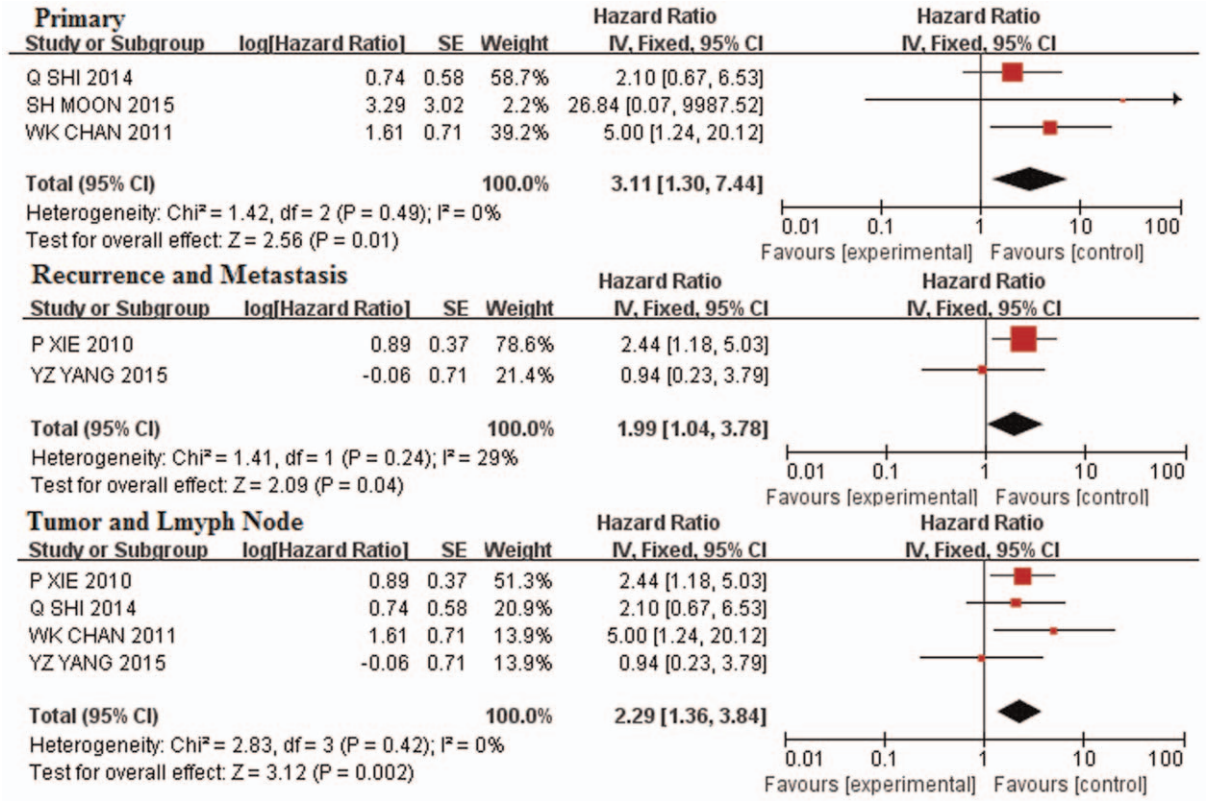

Figure 3. Subgroup of event-free survival of maximum standard uptake value.

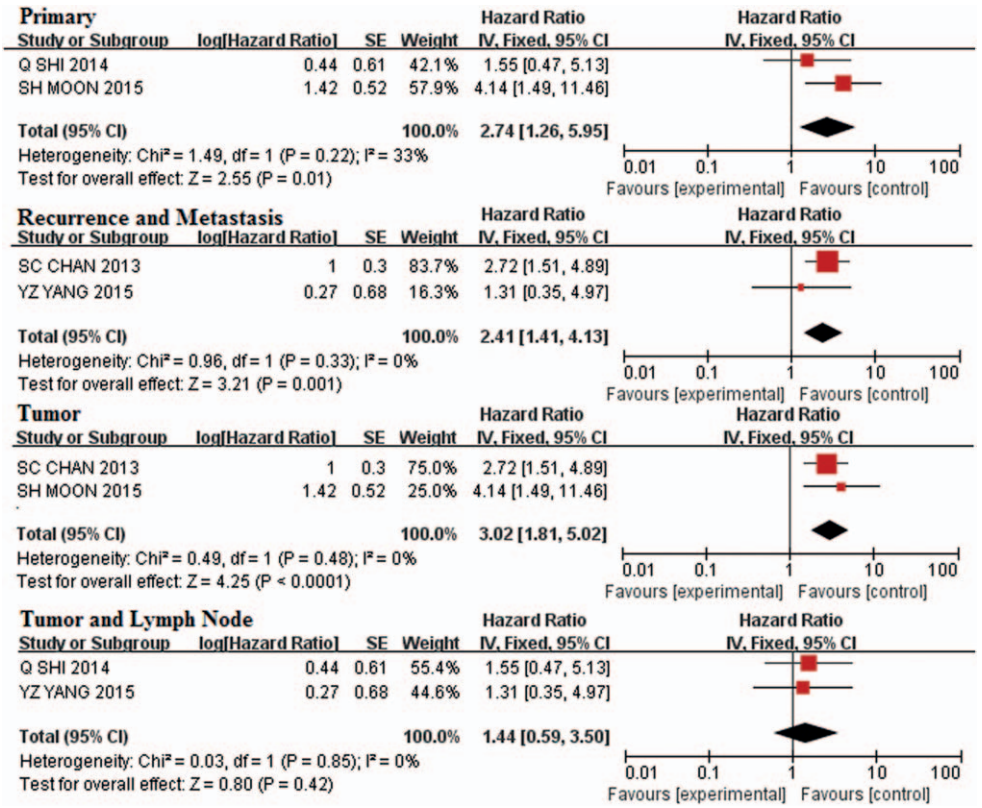

Figure 4. Subgroup of event-free survival OF metabolic tumor volume.

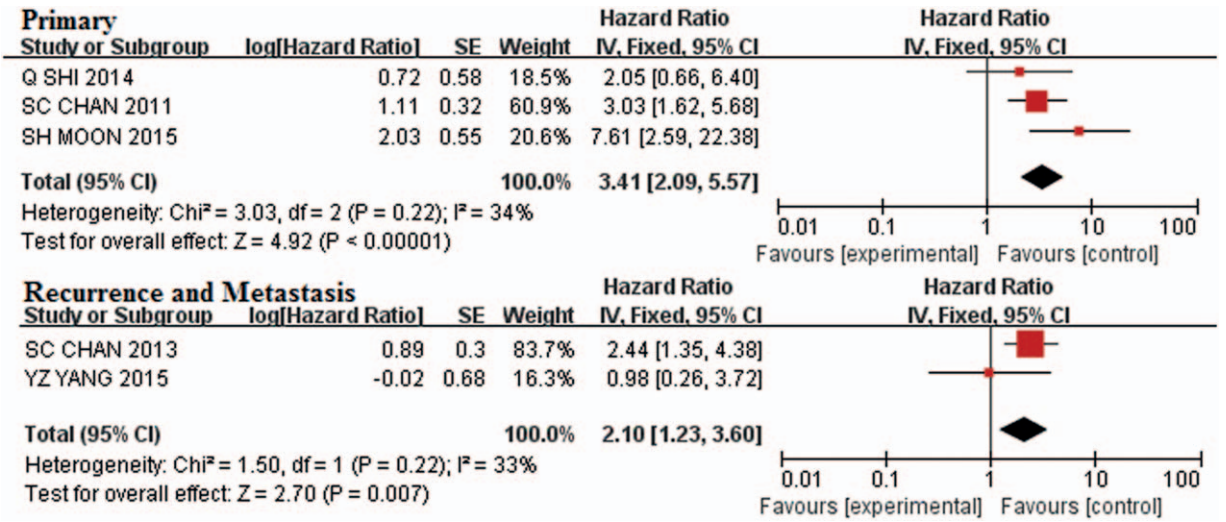

Figure 5. Subgroup of event-free survival of total lesion glycolysis.

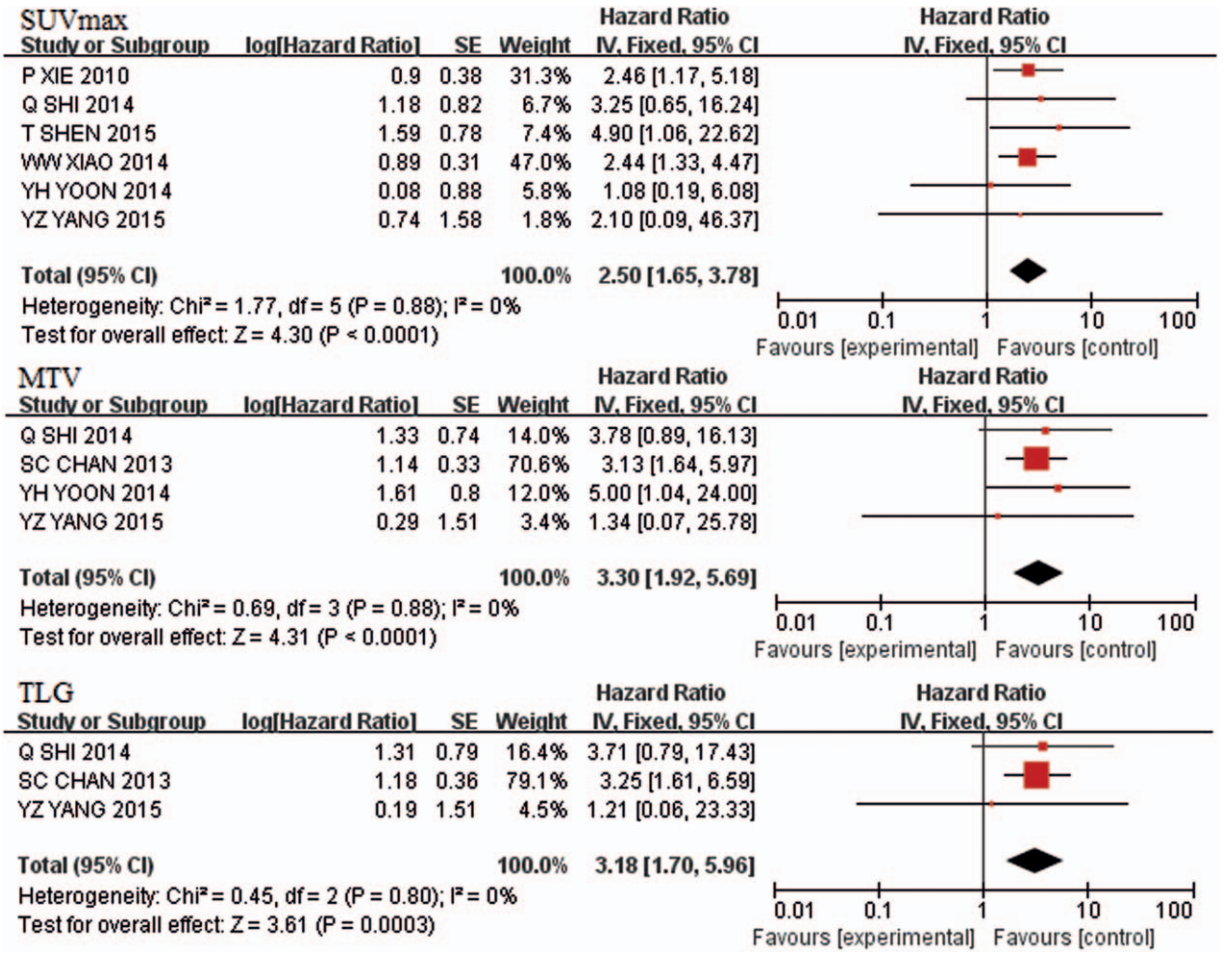

Figure 6. Forest plots of hazard ratio of overall survival of SUVmax, MTV, TLG. CI = confidence interval, MTV = metabolic tumor volume, SUVmax = maximum standard uptake value, TLG = total lesion glycolysis.

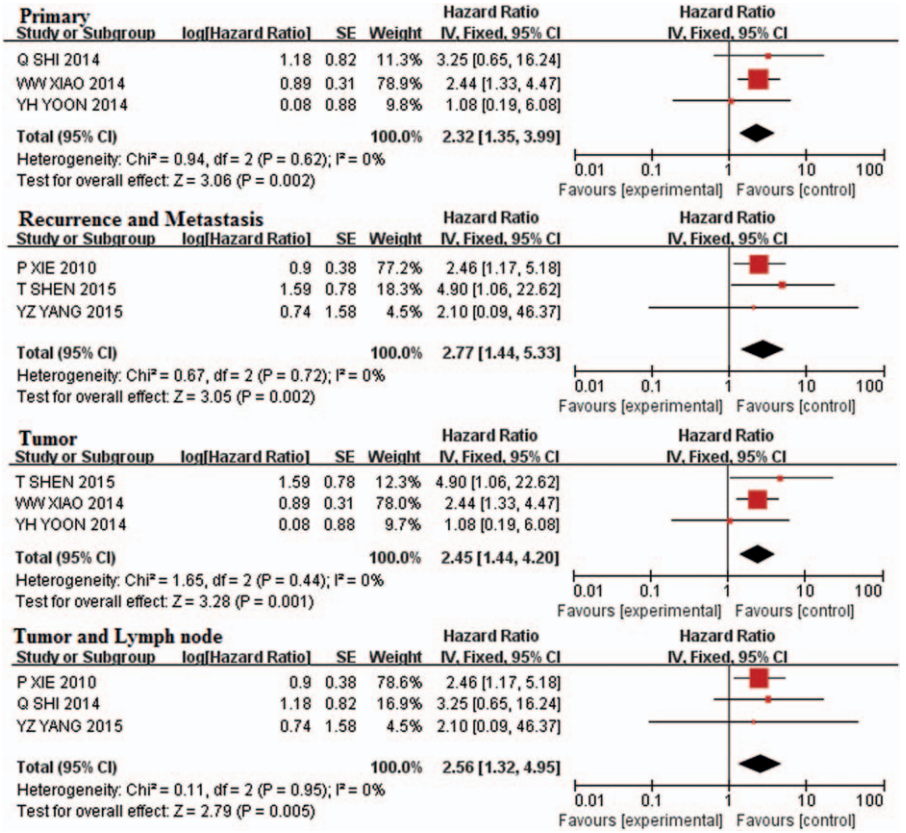

Figure 7. Subgroup of overall survival of maximum standard uptake value.

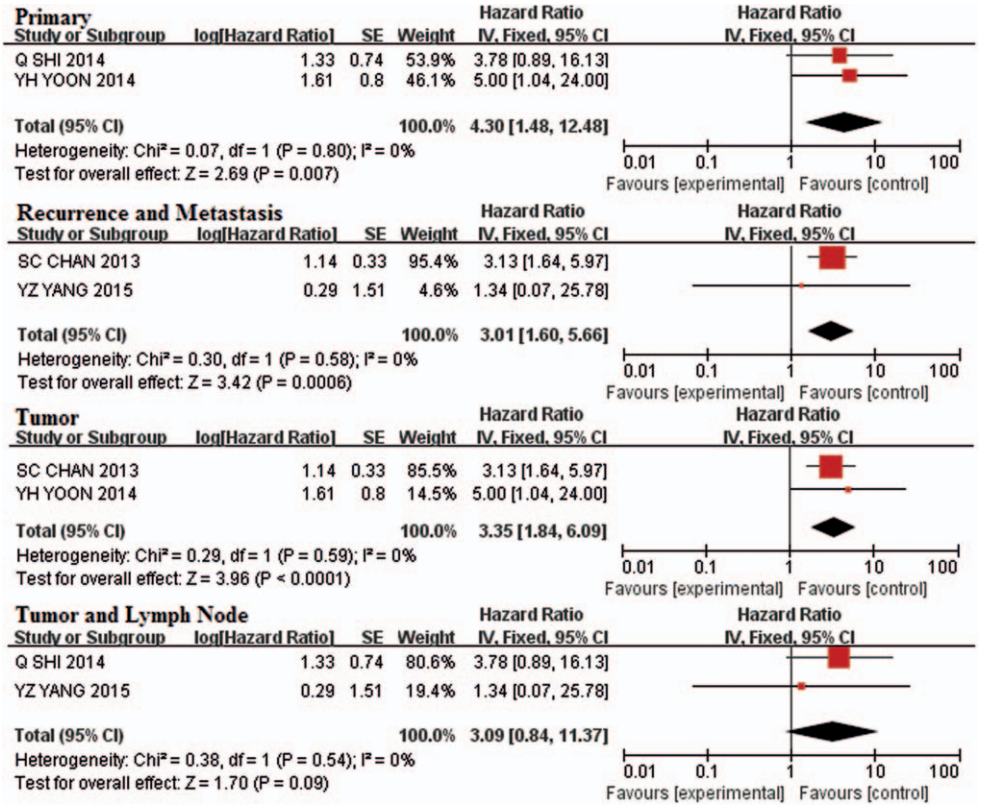

Figure 8. Subgroup of overall survival metabolic tumor volume.

Table 2

Summary of meta-analysis results.

		The number of articles	Survival outcome	HR (95% CI)	Heterogeneity (P, I^2)	Test for overall effect	Conclusion
SUVmax	Combined	5	EFS	2.33 (1.39–3.91)	P=.48; I^2=0%	0.001	Positive
	Tumor	1	EFS	26.84 (0.07–9987.52)	-	-	Positive
	Tumor+LN	4	EFS	2.29 (1.36–3.84)	P=.42; I^2=0%	0.002	Positive
	Primary	3	EFS	3.11 (1.30–7.44)	P=.49; I^2=0%	0.01	Positive
	Recurrence and metastasis	2	EFS	1.99 (1.03–3.78)	P=.24; I^2=29%	0.04	Positive
MTV	Combined	4	EFS	2.51 (1.62–3,.91)	P=.47; I^2=0%	<0.0001	Positive
	Tumor	2	EFS	3.02 (1.81–5.02)	P=.48; I^2=0%	<0.0001	Positive
	Tumor+LN	2	EFS	1.44 (0.59–3.40)	P=.85; I^2=0%	0.42	Negative
	Primary	2	EFS	2.74 (1.25–5.95)	P=.22; I^2=33%	0.01	Positive
	Recurrence and metastasis	2	EFS	2.41 (1.41–4.13)	P=.33; I^2=0%	0.001	Positive
TLG	Combined	5	EFS	2.74 (1.91–3.93)	P=.18; I^2=36%	<0.00001	Positive
	Primary	3	EFS	3.41 (2.09–5.57)	P=.22; I^2=34%	<0.00001	Positive
	Recurrence and metastasis	2	EFS	2.10 (1.23–3.60)	P=.22; I^2=33%	0.007	Positive
SUVmax	Combined	6	OS	2.50 (1.65–3.78)	P=.88; I^2=0%	<0.0001	Positive
	Tumor	3	OS	2.45 (1.44–4.20)	P=.44; I^2=0%	0.001	Positive
	Tumor+LN	3	OS	2.56 (1.32–4.95)	P=.95; I^2=0%	0.005	Positive
	Primary	3	OS	2.32 (1.35–3.99)	P=.62; I^2=0%	0.002	Positive
	Recurrence and metastasis	3	OS	2.77 (1.44–5.33)	P=.72; I^2=0%	0.002	Positive
MTV	Combined	4	OS	3.30 (1.92–5.69)	P=.88; I^2=0%	<0.0001	Positive
	Tumor	2	OS	3.35 (1.84–6.09)	P=.59; I^2=0%	<0.0001	Positive
	Tumor+LN	2	OS	3.09 (0.84–11.37)	P=.54; I^2=0%	0.09	Negative
	Primary	2	OS	4.30 (1.48–12.48)	P=.80; I^2=0%	0.007	Positive
	Recurrence and metastasis	2	OS	3.01 (1.60–5.66)	P=.58; I^2=0%	0.0006	Positive
TLG	Combined	3	OS	3.18 (1.70–5.96)	P=.80; I^2=0%	0.0003	Positive

CI=confidence interval, EFS=event-free survival, HR=hazard ratio, LN=lymph node, MTV=metabolic tumor volume, OS=overall survival, SUVmax=maximum standard uptake value, TLG=total lesion glycolysis.

also did a meta-analysis reporting that higher TLG and MTV predicted worse prognosis in HNC.

We carried out subgroup analyses to assess the prognostic effects of methods selected in each part on outcome (Table 2). The VOI was defined as whether is tumors alone or tumors and lymph node. Variable methods were used to measure VOI. And the value of VOI will be affected by the various measure methods. A settled SUV of 2.5 was adopted in 8 of 10 studies in the meta-analysis, which may be a criterion standard of threshold of VOI delineation. And this method was also used to measure TLG and MTV. In the subgroup delimited by the tumor, the HRs of SUVmax and MTV for EFS and OS were statistically significant. In the subgroup delimited by the tumor and lymph node, the HRs of SUVmax for EFS and OS were statistically significant, whereas the HRs of MTV were not. When the subgroup analysis was based on the stage of the tumor, all the HRs of SUVmax, MTV, and TLG for EFS and OS were statistically significant. And we could conclude that, for EFS, SUVmax and TLG might better predict the prognosis of patients with primary tumor than the patients with recurrence or metastasis. And for OS, MTV might have a stronger prognostic effect for patients with primary tumor.

Although SUVmax was reported earlier than MTV and TLG as an independent prognosis marker,[40] SUVmax was reported to be an independent prognostic marker in only 1 of 7 studies in non-small-cell lung cancer.[21] TLG weights the volumetric burden and metabolic activity of tumors and it seems a more accurate prognosis maker. But the number of published articles of TLG was less than that of SUVmax and MTV. The evidence of TLG and SUVmax helping predict the prognosis of the NPC patients should be accumulated and follow-up should be persistent. The included articles have adopted different VOI which could cause bias. In the future, more prospective studies are needed to be done. In this meta-analysis, all the data of patients were extracted before the therapy. Zhao et al[27] reported that the decrease of FDG uptake after therapy was connected to both EFS and OS in cervical cancer. They also reported that the decrease of the parameters was connected to the sensitivity of the therapy and these led to favorable prognosis in the patients with higher sensitivity. So the change of the SUVmax, MTV, and TLG after treatment needs to be investigated in the future research in NPC. Another article reported that high levels of pre-SBRT SUVmax of patients had poorer overall survival and local control and higher risk of distant metastases in non-small cell lung cancer.[41] What's more, the pretreatment SUVmax, MTV, and TLG of RT or IMRT can be studied in over survival in NPC. As mentioned above, the degree of research heterogeneity changed slightly after we introduced sensitivity analysis. The tumor grade, the cutoff value, and the variations in study quality may be connected to the heterogeneity.

However, there are several limitations in this meta-analysis. First, this research was based on a small numbers of patients. And only 941 patients were included in this study. Second, only the published data can be reached. Some significant negative data might not be published. Because of the amount of unpublished data, there may be publication bias in the meta-analysis, thus influencing the predicting value of the volumetric parameters. Third, only English articles were brought into our search. Articles written in other languages were not included. Fourth, the cutoff values were various. But so far, there is no criterion standard to define the cutoff value.

In conclusion, our meta-analysis presented that low values of SUVmax, MTV, and TLG concluded from the pretreatment PET/CT predicted a lower risk of recurrence and metastasis or death in NPC. PET/CT can be used in discovering the risk of metastasis and survival in NPC. Patients with NPC whose volumetric parameters are in high level should focus on the progress of the

tumor and the doctors should pay attention to the patients of high value of SUVmax, MTV, and TLG.

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