Using 18F-FDG PET/CT to Predict Esophageal Cancer Survival: A Meta-analysis

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Abstract

Background: This study aimed to explore whether metabolic responses to positron emission tomography/computed tomography (PET/CT) collected before, during, or after the treatment can predict the long-term survival rate of patients with esophageal cancer.

Main body: We searched for the following indices in articles listed in English and Chinese literature databases: the maximum standard uptake value (SUV\text{max}), mean standard uptake value (SUV\text{mean}), metabolic tumor volume (MTV), and total lesion glycolysis (TLG). If their values exceeded the thresholds, we defined them as responders; if they did not, we defined them as non-responders. We then performed a meta-analysis by extracting the hazard ratio (HR) and 95% confidence interval (95% CI) from each report to predict whether the status of responder or non-responder had an impact on prognosis.

We identified 34 articles with a combined sample size of 2794 patients. HRs and 95% CIs were measured as follows: SUV\text{max} = 1.15 (0.98-1.35), MTV = 3.45 (0.78-15.25), TLG = 1.04 (1.02-1.07), and SUV\text{mean} = 1.85 (1.33-2.57) (before treatment); ΔSUV\text{max} = 1.22 (1.06-1.39), Δ MTV = 1.07 (0.54-2.15), and
$\Delta TLG = 1.09 (0.59-2.02)$ (during treatment); and $SUV_{\text{max}} = 1.13 (1.05-1.22)$

and $TLG = 1.05 (1.02-1.09)$ (after treatment). The results showed that the

overall survival of the patients with low SUV (MTV, TLG) values was

significantly higher than that of the patients with high SUV (MTV, TLG) values.

**Conclusions:** This meta-analysis shows that the prognoses of patients with

PET metabolic responses are significantly better than those of non-responders.

Our findings may help inform the clinical treatment and prediction of the

prognoses of patients with esophageal cancer.

**Keywords:** positron emission tomography; esophageal neoplasms;

chemoradiotherapy

**Introduction**

Likely due to differences in economic development and living habits, the

incidence of upper gastrointestinal cancer is high in economically

underdeveloped areas, especially in East Asia and East Africa; for example,

the annual incidence of upper gastrointestinal cancer in China accounts for

44.6% of the global incidence of the disease [1]. Esophageal cancer is one of

the most common tumors of the upper digestive system. It is principally treated

with a combination of surgery and neoadjuvant or traditional radiotherapy and

chemotherapy. While this multimodal treatment has greatly reduced the
mortality and improved the disease-free survival rate of patients with esophageal cancer, the accurate prediction of the prognoses of patients following the treatment has remained a challenge. A superb supplement to traditional medical imaging, positron emission tomography (PET) has partially replaced invasive examinations such as endoscopic biopsy as a method of delineating the target area in the early stages of tumor radiotherapy and thus holds a potential for improving the prediction of a patient’s response to radiotherapy, chemotherapy, and even surgery.

In the past, CT was typically used to stage esophageal cancer. However, CT scans were not as useful 40 years ago as they are now. Despite its regional limitation, endoscopic ultrasound has become the best staging method. New tools are still needed to predict the prognosis of esophageal cancer [2]. \(^{18}\)F-fluorodeoxyglucose (FDG) PET has recently gained popularity as a metabolic imaging modality. Many researchers have used it to evaluate the efficacy or to predict the outcomes of radiotherapy, chemotherapy, and surgery; FDG PET can thus help avoid the prescription of ineffective or unnecessary treatments. We identified responders as patients with higher standard uptake value (SUV) values before treatment and lower SUV values after treatment, as well as patients with greater differences in SUV values before and after treatment. The values of PET parameters used as response
thresholds differ greatly, and most are based on experience; due to these

differences between articles, we have not listed the thresholds here.

As the literature featured no standardized guidelines, what changes in
PET parameters across treatment are considered to indicate prognosis vary.

Further, whether PET can predict the mortality and disease-free survival rate of
patients remains controversial. To help inform the resolution of this controversy
and contribute to a reference for clinical practice, the present meta-analysis of
all relevant and available literature aimed to conduct a systematic, objective
analysis of PET factors predictive of survival following esophageal cancer.

Methods

Literature search

We searched the Cochrane library MEDLINE, EMBASE, and China
National Knowledge Internet for documents published in Chinese or English
from any year. The following search query was used: “esophageal cancer” OR
“carcinoma of esophagus” OR “esophageal carcinoma” OR “esophagus
cancer” AND “positron emission tomography” OR “PET” AND “18F-FDG” OR
“fluorodeoxyglucose” AND “prognosis” OR “outcome” OR “prognostic” OR
“existence” OR “survival” OR “predict” (Fig 1).

Selection of studies
The selected articles were independently evaluated by four researchers (three clinical doctors and one professor of statistics) who did not communicate with one another. Scores were tallied out of 36 points. Clear mention of indices in the article earned 2 points, unclear mention of indices earned 1 point, and no mention of indices earned 0 points (or based on the explanation in the comments). The average of the four scores awarded by the researchers was used as the final score. Disagreements were settled through discussion (Table 1). Further details regarding the method used to score each article are described in the Appendix.

**Table 1.** standard for evaluation

| Project | Specific meaning | Comments |
|---------|-----------------|----------|
| 1       | Clearly define the research object |          |
| 2       | Study types     | Prospective (2) |
|         |                 | Retrospective (1) |
| 3       | Clearly define the outcome of the event | The optimal number of samples (2) |
|         |                 | Define the number of samples (1) |
| 4       | Application of statistical methods |          |
| 5       | Description of Statistical method |          |
| 6       | Criteria of patient included |          |
| 7       | Characteristics of patient included |          |
| 8       | Medical regulation and nursing convention |          |
| 9       | Description of treatment |          |
10 Number and reasons of excluded patients

11 follow-up period Including description of endings

12 Univariate survival analysis of prognostic factors There is direct HR and 95% CI (2)

There is no direct HR or 95% CI (1)

There is no way we can calculate HR (0)

13 Multivariate survival analysis of prognostic factors There is direct HR and 95% CI (2)

There is no direct HR or 95% CI (1)

There is no way we can calculate HR (0)

14 PET report: Basic Information

15 $^{18}$FDG-PET data acquisition

16 $^{18}$FDG-PET technical parameters

17 Using the double-blind method

18 Clearly defined threshold

HR, hazard ratio; CI, confidence interval

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110 Statistical methods
This paper selected four indices in each report to distinguish whether responding depends on each author's experience or practical results: the maximum standard uptake value ($SUV_{\text{max}}$), mean standard uptake value ($SUV_{\text{mean}}$), metabolic tumor volume (MTV), and total lesion glycolysis (TLG).

When merging statistical results, it was necessary to perform a heterogeneity test to judge whether the statistics were heterogeneous. P-values of $\leq 0.100$ were considered to indicate heterogenous statistical results.

In Revman software, $I^2$ can be used to describe the percentage of heterogeneity caused by various studies rather than sampling errors in the total heterogeneity. The formula used to calculate $I^2$ is as follows:

$$I^2 = \frac{Q - (k - 1)}{Q} \times 100\%$$

where $Q$ represents the chi-square value ($\chi^2$) of the heterogeneity test, and $k$ represents the number of included studies. $I^2$ values of $\leq 50\%$ were considered to indicate statistical significance. The values of the four indicators of the survival rate selected in these papers were generated by the comparison of the overall survival (OS) rate, as calculated from the hazards ratio (HR) and 95% confidence interval (CI), between the two groups. The HR was calculated with the following formula:

$$pooled \ln HR = \left[ \frac{\sum \text{logrank Observed - Expected events}(O - E)}{\sum \text{log rank Variance}(V)} \right]$$
If HR and variance (V) were mentioned in the original text, they could be directly applied to the meta-analysis. The method of Jayne et al. [4] can be used to calculate the HR and 95% CI in any case from the K-M curve and P-value. First, the approximate value of each point on the curve is obtained by using Engauge Digitizer, and the approximate value of HR is calculated from the Excel table accompanying the manuscript published by Jayne et al. Revman is then used to calculate the upper and lower intervals of the 95% CI.

If there are no censored data, the following formula can be used:

\[
\text{pooled } \ln \text{HR} = \left[ \frac{\sum \ln \text{HR}}{\sum \frac{1}{\text{Variance of the } \ln \text{HR}}} \right]
\]

The survival rate of patients with low SUV values (low MTV values/TLG values or high absolute value of ΔSUV) is generally higher than that of patients with high SUV values when HR > 1.0. By contrast, the survival rate of patients with high SUV values (high MTV value/TLG value or low absolute value of ΔSUV) is higher than that of patients with low SUV values when HR ≤ 1.0.

If the results featured bias, we considered the subgroups analysis to confirm the presence of publication bias.
All the data were analyzed with Revman5.0 (The Nordic Cochrane Centre, Copenhagen, Denmark), MetaXL5.3 (EpiGear International Pty Ltd, Queensland, Australia), and Stata15.1 (StataCorp, Lakeway Drive, College Station, Texas, USA).

Results

Study selection and characteristics analysis

Hundreds of articles were retrieved from the aforementioned databases. After reading the titles and abstracts, 105 related articles were selected for analysis. Articles were subsequently removed on account of the following: 1) contents were unrelated to the target results, 2) extracting the HR and 95% CI was impossible, 3) the article was published more than once by the same author, or 4) the study used other treatments or monitoring methods that interfered with the extraction of the target results. Finally, 34 articles remained. Articles containing only some of the target results and those featuring all of the target information were extracted separately. Of these 34 articles, 24 considered the effect of SUV\textsubscript{max} before treatment[5-28]; nine, MTV before treatment[16, 20, 22, 24-26, 28-31]; seven, TLG before treatment[20, 21, 25, 26, 28, 29, 31]; three, SUV\textsubscript{mean} on OS before treatment[21, 22, 25]; four, SUV\textsubscript{max} after treatment[7, 13, 17, 26, 28, 32]; three, TLG after treatment[26, 28, 32]; 10, the effect of ΔSUV\textsubscript{max} before and after treatment[13, 17, 23, 26, 28, 33-]
four, ΔMTV before and after treatment[26, 28, 36, 38]; and five, effect of ΔTLG before and after treatment (Tables 2 and 3)[22, 26, 28, 36, 38].

| Project | Specific meaning                                      | Comments                                         |
|---------|-----------------------------------------------------|-------------------------------------------------|
| 1       | Clearly define the research object                  |                                                 |
| 2       | Study types                                         | Prospective (2)                                 |
|         |                                                     | Retrospective (1)                               |
| 3       | Clearly define the outcome of the event             | The optimal number of samples (2)               |
|         |                                                     | Define the number of samples (1)                |
| 4       | Application of statistical methods                  |                                                 |
| 5       | Description of Statistical method                   |                                                 |
| 6       | Criteria of patient included                        |                                                 |
| 7       | Characteristics of patient included                 |                                                 |
| 8       | Medical regulation and nursing convention           |                                                 |
| 9       | Description of treatment                            |                                                 |
| 10      | Number and reasons of excluded patients             |                                                 |
| 11      | follow-up period                                    | Including description of endings                |
| 12      | Univariate survival analysis of prognostic factors  | There is direct HR and 95% CI (2)               |
|         |                                                     | There is no direct HR or 95% CI (1)             |
|         |                                                     | There is no way we can calculate HR (0)         |
Multivariate survival analysis of prognostic factors

| Line | Description |
|------|-------------|
| 13   | There is direct HR and 95% CI (2) |
|      | There is no direct HR or 95% CI (1) |
|      | There is no way we can calculate HR (0) |

PET report: Basic Information

18FDG-PET data acquisition

18FDG-PET technical parameters

Using the double-blind method

Clearly defined threshold

| Line | Description |
|------|-------------|
| 14   | PET report: Basic Information |
| 15   | 18FDG-PET data acquisition |
| 16   | 18FDG-PET technical parameters |
| 17   | Using the double-blind method |
| 18   | Clearly defined threshold |

HR, hazard ratio; CI, confidence interval

Quality assessment

The lowest quality score of the 34 selected articles was 39, and the highest was 84. The scoring system adopted by the reviewers was relatively strict, and the document quality was relatively high. If an article lacked necessary information, the corresponding author of the article was contacted.

Meta-analysis

A meta-analysis of the four indicators ($SUV_{\text{max}}$, $SUV_{\text{mean}}$, MTV, and TLG) before treatment was performed for OS. Twenty-four articles included the
SUV$_{\text{max}}$. Because the I$^2 = 82\% > 50\%$, these articles were analyzed with the QE model (HR = 1.15, 95% CI = 0.98-1.35). The results showed that the OS of the patients with low SUV$_{\text{max}}$ was significantly higher than that of the patients with a high SUV$_{\text{max}}$ (Fig. 2A, 2B, 2C).

The asymmetry of the funnel chart suggested publication bias. The two methods of Begg and Egger of Stata used to detect the publication bias indicated contradictory results. For a small sample, the Egger method (Fig. 3A) is more sensitive than the Begg (Fig. 3B) method. The result of P = 0.000 indicated that the selected articles were subject to publication bias.

Because of the large heterogeneity, we performed subgroup analyses. The patients were categorized according to the following pathological types (articles that did not mention pathological types were excluded): squamous cell carcinoma, adenocarcinoma, and unsegmented. The HR and 95% CI of each subgroup were 3.69 (1.68-8.09), 0.96 (0.89-1.04), and 1.41 (1.16-1.71), respectively. These values were significantly different (p<0.00001).

The patients were further categorized according to the pathological stage of their cancer (articles that did not mention the stage were excluded): stage III or earlier, and stage IV or earlier. The HR and 95% CI of each subgroup were 2.35 (1.59-3.48) and 1.52 (1.17-1.97), respectively. There was no significant difference between the two groups (p=0.07).
The patients were also divided according to treatment: radiotherapy and chemotherapy (S), operation (O), and undifferentiated treatment (N). The HR and 95% CI of each subgroup were 1.63 (1.32-2.02), 2.07 (1.20-3.55), and 1.19 (0.95-1.49), respectively. No significant difference was found between the three groups (P = 0.06, Fig. 4A, 4B, 4C).

Nine articles included in our analysis considered MTV. Because the $I^2 = 100\% > 50\%$, these articles were analyzed with the QE model (HR = 3.45, 95% CI = 0.78-15.25). Our results showed that the OS of the patients with low MTV values was significantly higher than that of the patients with high MTV values.

Seven articles included in our analysis considered TLG. Because the $I^2 = 81\% > 50\%$, these articles were analyzed with the QE model (HR = 1.04, 95% CI = 1.02-1.07). The results showed that the OS of the patients with low TLG values was significantly higher than that of the patients with high TLG values.

Three articles included in our analysis considered the SUV$_{\text{mean}}$. Because the $I^2 = 48\% < 50\%$, these articles were analyzed with the fixed-effect model (HR = 1.85, 95% CI = 1.33-2.57). The results showed that the OS of the patients with low SUV$_{\text{mean}}$ scores was significantly higher than that of the patients with high SUV$_{\text{mean}}$ scores.

Meta-analysis of the three indicators ($\Delta$ SUV$_{\text{max}}$, $\Delta$ MTV, and $\Delta$ TLG) measured during treatment was performed. Ten articles included in our
analysis considered the $\Delta S_{\text{max}}$. Because the $I^2 = 48\% < 50\%$, these articles were analyzed with the fixed-effect model ($HR = 1.22$, 95%CI = 1.06-1.39). The results showed that the OS of the patients with high absolute values of $\Delta S_{\text{max}}$ was significantly higher than that of the patients with low absolute values of $\Delta S_{\text{max}}$.

Four articles included in our analysis considered the $\Delta \text{MTV}$. Because the $I^2 = 90\% > 50\%$, these articles were analyzed with the QE model ($HR = 1.07$, 95% CI = 0.54-2.15). The results showed that the OS of patients with high absolute values of $\Delta \text{MTV}$ was significantly higher than that of the patients with low absolute values of $\Delta \text{MTV}$.

Five articles included in our analysis considered the $\Delta \text{TLG}$. Because the $I^2 = 87\% > 50\%$, these articles were analyzed with the QE model ($HR = 1.09$, 95% CI = 0.59-2.02). The results showed that the OS of the patients with high absolute values of $\Delta \text{TLG}$ was significantly higher than that of the patients with low absolute values of $\Delta \text{TLG}$.

Meta-analysis of the two indicators ($S_{\text{max}}$ and TLG) measured after treatment was performed. Six articles included in our analysis considered the $S_{\text{max}}$. Because the $I^2 = 58\% > 50\%$, these articles were analyzed with the QE model ($HR = 1.13$, 95% CI = 1.05-1.22). The results showed that the OS of
the patients with low $\text{SUV}_{\text{max}}$ values was significantly higher than that of the patients with high $\text{SUV}_{\text{max}}$ values.

Three articles included in our analysis considered TLG. Because the $I^2 = 91\% > 50\%$, these articles were analyzed with the QE model (HR = 1.05, 95% CI = 1.02–1.09). The results showed that the OS of the patients with low TLG values was significantly higher than that of the patients with high TLG values.

Discussion

The sixth leading cause of cancer-related death and the eighth most common cancer in the world, esophageal cancer is associated with a 5-year survival rate of less than 25% [39]. While endoscopy, CT, and MRI have conventionally been used to examine patients with esophageal cancer, the relatively new technique of PET has been increasingly used for the diagnosis, differential diagnosis, and clinical staging of patients with esophageal cancer. Imaging also helps to identify patients with significant complications who may respond to and benefit from more conservative treatment (i.e., without esophagectomy) after CRT is demonstrated to be fully or partially effective. Finally, PET/CT has demonstrated value as a follow-up tool for the timely detection of tumor recurrence after surgical treatment [40]. However, because $^{18}\text{F}-\text{FDG}$PET can help to inform the metabolic diagnosis of esophageal cancer, it can compensate for the shortcomings of traditional methods and predict the
prognosis of patients when combined with CT to construct a clear anatomical image. A study found $^{18}$F-FDG PET/CT to be a powerful prognostic tool for evaluating OS in patients with esophageal cancer before, during, or after chemoradiation (CTRT). PET parameters (TLG = 50) can guide future treatment strategies by stratifying stage II/III patients who will receive CTRT according to their predicted OS [41]. Another study showed that PET could reflect the response of esophageal cancer to neoadjuvant chemotherapy: the SUV values of the PET responders were significantly higher than those of the PET non-responders [42]. However, SUV changes and PET responses were not found by the study to be associated with prognosis.

The articles selected in this meta-analysis featured considerable heterogeneity. The use of the traditional RE model and the square of tau ($\tau^2$) to measure the differences between studies indicated large variance in the results of small samples, which leads to small weights. When calculating the weights in each study, the same $\tau^2$ values are used for the denominators; hence, small studies will contribute a disproportionately large weight, while the weight of large studies will be reduced. The QE model is used to resolve the drawback of the RE model.

For cases with large heterogeneity, subgroup analysis was used to identify the source of heterogeneity. For studies providing the SUV$_{\text{max}}$ before treatment, the possible causes of heterogeneity include, sex, age, treatment
plan, clinical stage, pathological type, sample size, and article quality scores.

However, as most articles did not make a clear distinction between sex and age, the present meta-analysis considered the patient's treatment plan, clinical stage, and pathological type as sources of heterogeneity.

When the patients were divided according to pathological type, the value of SUV$_{\text{max}}$ could predict the OS of patients with squamous cell carcinoma and undifferentiated pathologies but not for those with adenocarcinoma pathologies. The difference between the three groups was statistically significant, indicating that the relationships between pathological type, the value of SUV$_{\text{max}}$, and OS are unclear and that the $^{18}$F-FDG uptake of adenocarcinoma cells is not as effective as that of squamous cells (low or no uptake can be seen in 10% to 15% of undifferentiated adenocarcinomas). Hence, caution should be exercised when using the SUV$_{\text{max}}$ to predict the OS of patients whose esophageal cancer follows the pathological pattern of adenocarcinomas.

When subgroups were divided according to stage, we found no significant difference between patients with cancer before or at stage III and those with cancer before or at stage IV. However, it is possible that SUV$_{\text{max}}$ is more effective as a predictor of esophageal cancer in the early and middle stages of cancer because the group of patients with cancer before or at stage IV...
includes patients with cancer before or at stage III. More experiments are needed to confirm this hypothesis.

When the patients were sorted according to treatment, we found no significant difference between the four groups. While the methods of radiotherapy and chemotherapy, drug use, radiation dose, target delineation, and even surgical methods differed among the reviewed studies, the analyses of each subgroup confirmed that $SUV_{\text{max}}$ could still be used to predict OS.

The overall analysis revealed that regardless of whether the indices were measured before or after treatment, $SUV_{\text{max}}$, MTV, TLG, and $SUV_{\text{mean}}$ could perform well in predicting the OS of patients; the value of MTV is related to the size of the solid tumor, while the values of $SUV_{\text{max}}$ and TLG are related to the pathological response. Hence, $SUV_{\text{max}}$ and TLG can directly predict the efficacy of radiotherapy, chemotherapy, and surgery.

This report is subject to several limitations. First, many of the included articles did not directly report HR values but instead extracted them through the K-M curve. This method inevitably results in mistakes. Second, the funnel chart of the reports collected from the literature was subject to publication bias, likely resulting in the overestimation of the presently identified predictive effect of the indices. Finally, all of the reports sourced from the literature are case-control or cohort studies, highlighting the need for large randomized controlled
trials of the potential of PET/CT for predicting the prognoses of patients with esophageal cancer.

Conclusion

Although our study is subject to limitations, it demonstrates that the prognoses of patients who respond to PET are significantly better than those of non-responders. Hence, our study can help to inform the prediction of the prognoses of patients with esophageal cancer and, therefore, their treatment.

List of abbreviations

\(^{18}\text{F-fluorodeoxyglucose: FDG}\)

95% confidence interval: 95% CI

Chemoradiation: CTRT

Hazard ratio: HR

Maximum standard uptake value: SUV\text{max}

Mean standard uptake value: SUV\text{mean}

Metabolic tumor volume: MTV

Overall survival: OS

Positron emission tomography/computed tomography: PET/CT
Total lesion glycolysis: TLG

**Declarations**

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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

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Authors’ contributions: JW conducted data curation, performed formal analysis, and wrote this paper. JS managed conceptualization and project administration. SL constructed the methodology, and reviewed and edited the paper.

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**Table 3.** Indices from the studies in the meta-analysis

| Study     | Index | Time                        | Threshold                          |
|-----------|-------|-----------------------------|------------------------------------|
| Nakajo2016| SUVmax| Before Chemoradiotherapy    | NM                                 |
|           | SUVmin| Before Chemoradiotherapy    |                                    |
|           | MTV TLG|                             |                                    |
| Butof2015 | SUVmax| Before radiotherapy         | SUVmax>8.5 SUVmean>8.14             |
|           | SUVmin|                             | MTV>8.5 TLG>12.4                   |
|           | MTV TLG|                             |                                    |
| Rebecca2018| SUV MTV TLG| Before and after Chemoradiotherapy | Pre:SUV>13.4 MTV>26.3 TLG>121   |
|           |       |                             | Post:SUV>5.33 MTV>6.6 TLG>30.2     |
|           |       |                             | Δ SUV >38.8% Δ MTV >35%            |
|           |       |                             | Δ TLG>38.8%                       |
| Hamai2016 | SUVmax| Before and after Chemoradiotherapy | Post:SUVmax>5.33 Δ SUVmax>75% |
| Kauppi2012| SUV   | Before and after Chemoradiotherapy | Pre:SUVNM Post:SUVNM |
|           |       |                             | Δ SUV >67%                        |
| Li2019    | SUVmax| Before and after radiotherapy | Pre:SUVmax>9.6 MTV>10.5 TLG>59.8  |
|           | MTV TLG|                             | Post:SUVmax>7.8 MTV>15.9 TLG>44.3 |
|           |       |                             | Δ SUVmax>23% Δ MTV>7.5%            |
|           |       |                             | Δ TLG>27%                         |
| Huang2016 | SUVmax| Before radiotherapy         | SUVmax>9.7                        |
| Xie2014   | SUVmax| Before radiotherapy         | SUVmax>11.4                       |
|           | MTV TLG|                             | MTV≥8.27 TLG≥35.21                |
| Risk2006  | SUVmax| before operation            | SUVmax>4.5                        |
| Chang2016 | SUVmax| before Chemoradiotherapy    | SUVmax>4.86 SUVmean>2.37          |
|           | SUVmean|                             | MTV>8.93 TLG>20.42                |
| Study          | Index   | Time                          | Threshold       |
|---------------|---------|-------------------------------|-----------------|
| Rest2008      | SUVmax  | before operation              | SUVmax>9        |
| Dai2018       | SUVmax  | Before treatment              | SUVmax>6        |
| Hiasa2014     | SUVmax  | Before treatment              | SUVmax>10.26    |
| Toru1993      | SUV     | before operation              | SUV≥7.0         |
| Cerfolio2006  | SUV     | before operation              | SUV≥6.6         |
| Chung2007     | SUV     | before operation              | SUV≥15          |
| Kato2002      | SUV     | before operation              | SUV≥3           |
| Lordick2007   | SUV     | Before and after treatment    | Δ SUV≥35%       |
| Ott2006       | SUV     | Before and after treatment    | Δ SUV≥35%       |
| Risk2009      | SUV     | Before and after treatment    | SUVmax≥4.5      |
| Roedl2008     | SUVmax  | Before and after treatment    | Δ SUVmax≥43%    |
|               | SUVmean | Before and after treatment    | Δ SUVmean≥22%   |
|               | MTV TLG | Before and after treatment    | Δ MTV≥63% Δ TLG≥78% |
| Swisher2004   | SUV     | Before and after Chemoradiotherapy | Pre:SUV>9.5 Post:SUV>4 |
| Heta2009      | SUV     | Before and after treatment    | Δ SUV>52%       |
| Heta2008      | SUV     | Before Chemoradiotherapy      | SUV>10.1        |
| Vanwestreenen2005 | SUVmax | Before treatment              | SUVmax≥6.7      |
| Author       | Parameter | Before and after treatment | Δ SUV ≥ 35% | SUV_{max} | MTV > 14.5 | NM | MTV ≥ 27.44 | TLG ≥ 166.2 | SUV_{max} > 11.6 | MTV > 14.5 | NM | MTV > 22.3 | TLG > 46 | Δ SUV ≥ 60% | Chemoradiotherapy | SUV NM | Δ SUV_{max} > 23.5 | Δ MTV > 25.5% | Δ TLG > 44.8% | NM | Δ SUV ≥ 35% | Chemoradiotherapy | NM | Δ SUV ≥ 35% | Chemoradiotherapy | NM |
|--------------|-----------|-----------------------------|-------------|-----------|------------|----|------------|-------------|------------------|------------|----|------------|---------|-------------|-------------------|-------|-----------------|-----------------|-----------------|----|-----------------|-------------------|----|-----------------|-------------------|----|
| Weber2001    | SUV       | Before and after Chemotherapy | Δ SUV ≥ 35% |           |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Zhu2011      | SUV_{max} | before operation            | SUV_{max} > 11.6 |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Yu2018       | MTV       | before operation            | NM          |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Lin2018      | MTV TLG   | before operation            | MTV ≥ 27.44 | TLG ≥ 166.2 |            |    |            |              |                  |            |    |            |         | 0            |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Hofheinz2019 | SUV       | Before Chemoradiotherapy    | MTV > 22.3  | TLG > 46   |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Huang2015    | SUV       | Before and after Chemoradiotherapy | Δ SUV > 60% |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Kim2016      | SUV_{max} | Before and after radiotherapy | Δ SUV_{max} > 23.5 |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Anna2014     | SUV       | after radiotherapy          | NM          |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |
| Yanagawa2012 | SUV       | Before and after chemotherapy | NM          |            |            |    |            |              |                  |            |    |            |         |              |                    |      |                 |                 |                |    |                 |                    |    |                 |                    |    |

NM, not mentioned; SUV_{max}, the maximum standard uptake value; SUV_{mean}, mean standard uptake value; MTV, metabolic tumor volume; TLG, total lesion glycolysis; Δ means differences before and after treatment.
Figure Legends

Figure 1 Flowchart of the selection of articles.

Figure 2 Forest plots of SUV\textsubscript{max} before treatment (A). Z-score of 24 studies before treatment (B). Funnel Plots of SUV\textsubscript{max} before treatment. These articles may be subject to publication bias (C). ES = effect size (hazard ratio), SUV\textsubscript{max} = the maximum standard uptake value.

Figure 3 Egger’s test of SUV\textsubscript{max} before treatment (A). Begg’s test of SUV\textsubscript{max} before treatment (B). SUV\textsubscript{max} = the maximum standard uptake value.

Figure 4 Forest plots of the SUV\textsubscript{max} subgroup according to pathological type (A), stage of cancer (B), and type of treatments (C). SUV\textsubscript{max} = the maximum standard uptake value.