18F-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography-Guided Chest Radiotherapy Improves Survival in Patients with Extracranial Oligometastatic Non-small Cell Lung Cancer

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Abstract

Background This retrospective study compared positron emission tomography (PET)/computed tomography (CT) and CT in the treatment of extracranial oligometastatic non-small-cell lung cancer (NSCLC) and explored the impact of chest radiotherapy (CRT) on patient survival.

Methods We reviewed the medical records of Chinese patients with stage IV extracranial oligometastatic NSCLC who underwent PET/CT or CT at two centers. Propensity score matching (PSM) was used to control differences in patient characteristics between the maintenance chemotherapy alone and CRT plus maintenance chemotherapy groups.

Results We analyzed 192 eligible patients. The median survival time was significantly longer in the CRT plus maintenance group than in the chemotherapy alone group (13 months vs. 8 months, $p < 0.001$). Subgroup analysis showed no statistical difference in survival between both groups in patients who underwent CT examinations ($n=98$, 8 months vs. 5 months, $p = 0.180$). However, differences in survival between both groups were statistically significant in patients who underwent PET/CT examinations ($n=94$, 25 months vs. 11 months, $p < 0.001$). A multifactorial analysis revealed a more favorable prognosis in patients who underwent PET/CT evaluation (HR: 0.343, 95% CI: 0.250-0.471, $p < 0.001$) and CRT (HR: 0.624, 95% CI: 0.464-0.840, $p = 0.002$) than in those who did not. The conclusion obtained after PSM is consistent with the above mentioned results.

Conclusions PET/CT-guided CRT is associated with improved clinical outcomes in patients with stage IV extracranial oligometastatic NSCLC.

1. Introduction

Oligometastasis is a distant metastasis with a limited number and distribution of tumors. Patients with oligometastasis usually have a maximum of 3-5 metastatic sites, excluding the primary site, and no more than 3 different organs that can be treated locally using surgery, radiation therapy, and other treatments to improve survival [1]. Currently, oligometastasis is considered to be the transitional stage of advanced tumors from inducing limited to extensive metastases, with the former metastases having a significantly different biology and treatment options than the latter metastases [2]. This is a shift from the conventional oncological thinking, which considers metastasis as an end-stage disease with limited treatment options. In patients with non-small-cell lung cancer (NSCLC) receiving systemic therapy, such as chemotherapy, the most common progression site is the original disease site [3-6]. Our previous studies have shown that aggressive local consolidation therapy may destroy lesions, slow disease progression, and even improve patient survival [7].

Radiation therapy is a local NSCLC treatment. The clinical outline of the gross tumor volume (GTV) is based on morphological information, such as tissue density and anatomical structure, as provided by computed tomography (CT), but not on corresponding metabolic information. Consequently, potential occult metastases are often not detected, and the information provided is not sufficient to allow clinical

radiation therapy[8]. ^{18}F -fluorodeoxyglucose positron emission tomography-CT (^{18}F FDG-PET /CT) is of great value for early lung cancer detection, differential diagnoses of isolated nodules in lungs and mediastinum lymph nodes, clinical staging and detection of distant metastases, treatment efficacy determination, recurrence and metastasis follow-ups, and prognosis [9, 10]. ^{18}F FDG, the most widely used PET imaging agent in clinical practice, is brought into the cell, and then ^{18}F FDG-PET imaging distinguishes between benign and malignant lesions based on glucose metabolism, which is significantly correlated with tumor pathological response [11]. Most lung cancers are highly metabolic in nature, and abnormal cancer cell proliferation requires glucose overutilization. Accordingly, ^{18}F FDG-PET/CT has the advantages of both functional and anatomical structure imaging. ^{18}F FDG-PET/CT is better than traditional imaging methods and is increasingly recognized by clinicians for the diagnosis, treatment, and treatment efficacy evaluation of lung cancer and other tumors [12-14].

We demonstrated that local consolidation therapy (LCT) is superior to maintenance therapy in patients with oligometastatic NSCLC receiving PET/CT guidance [7]. However, we did not directly compare lung cancer patients who underwent PET/CT to those who underwent conventional CT, and there is no direct evidence to confirm a significant difference in the prognostic benefit between these two screening methods in patients with oligometastatic NSCLC. Undertreatment may significantly contribute to treatment failure or tumor recurrence, but overtreatment can cause serious side effects and physical damage. Minimizing unnecessary treatment while ensuring efficacy is important for the survival and quality of life of patients with advanced lung cancer. To further improve the diagnosis and treatment of oligometastatic NSCLC, we retrospectively studied the medical records of patients with oligometastatic NSCLC who underwent PET/CT and conventional CT at two centers to investigate the differences between both examination methods and the impact of radiation therapy to the primary lung cancer site on patient prognosis.

2. Materials And Methods

2.1 Study population

We retrospectively analyzed Chinese patients with stage IV extracranial oligometastatic NSCLC who had undergone PET/CT or CT scans at the First Hospital of China Medical University and Liaoning Cancer Hospital from February 2013 to November 2019. From patient medical records, we assessed age, gender, smoking history, patient status, tumor size, lymphatic metastases, histologic type, primary tumor site, treatment choice, and date of death. Inclusion criteria were patients with extracranial oligometastatic NSCLC with complete medical records who received chest radiotherapy (CRT) with maintenance or only maintenance therapy. PET/CT or CT was conducted on selected patients within one month before treatment. Patients with major organ dysfunction, more than one primary tumor, unknown metastatic status, or multiple metastases (number of transferring stoves >5), malignant pleural effusion, or underwent targeted therapy or immunotherapy were excluded.

Propensity score matching (PSM, The PSM was performed using age and sex) was used to create a maintenance chemotherapy alone and a chest radiotherapy (CRT) plus maintenance chemotherapy groups to reduce the effects of selection bias and confounding variables. The PSM function of the IBM SPSS software (IBM Co., Armonk, NY, USA) was used to estimate the propensity score, and 1:1 nearest neighbor matching was used with a caliper width of 0.02 for PSM. A chi-square test was used to check the covariate balance of each subgroup before and after PSM.

2.2 Statistical analysis

The number and clinical characteristics of all eligible patients were counted, and the chi-square test was used. The time from each patient's first oligometastatic diagnosis to the last follow-up or death was recorded as overall survival time. The survival curves of different variables were determined using the kaplan-meier method and then checked by a log-rank test. Results were reported as hazard ratios (HRs) and 95% confidence intervals (CIs). Forest plots were used to describe the subgroup analysis of all data. According to the univariate analysis results, significant variables ($p < 0.1$) were selected and put into a Cox regression analysis and then a multivariate analysis to ensure that significant variables ($p < 0.05$) were remarkably associated with the prognosis of patients with extracranial oligometastatic NSCLC. IBM SPSS was used for statistical analysis, and GraphPad Prism8 was used to draw the survival curve and forest plots.

3. Results

3.1 Patient Characteristics

From analyses, 192 of a total of 532 patients with advanced lung cancer at two medical centers were selected; 113 patients were male, and 79 were female, with a median age of 60 years. We used PSM to select 178 eligible patients of 192 patients with extracranial oligometastatic NSCLC and divided them into maintenance chemotherapy alone and CRT plus maintenance chemotherapy groups (Figure 1).

Among all patients, the one-year and two-year overall survival rates were 41.7% and 15.1%, respectively, and the median survival time was 10.5 months. Patient demographic and clinical characteristics are presented in Table 1.

3.2 Univariate analysis

Considering tumor heterogeneity, we did not examine the relationship between different chemotherapy regimens and survival time. Important variables included in the univariate analysis before and after PSM, including T and N classifications, PET/CT and CRT are presented in Table 2 and 3 (all $p < 0.1$). The median survival time was better in patients who received PET/CT than in those who only received CT (before PSM: 16 months vs 6 months; and after PSM: 17 months vs 7 months, both, $p < 0.001$). The median survival time was significantly better in the CRT plus maintenance group than in the

chemotherapy alone group (before PSM: 13 months vs 8 months, $p < 0.001$; and after PSM: 13 months vs 8 months, both, $p = 0.001$).

3.3 Survival analysis and subgroup analysis

Figure 2 and Figure 3 showed that PET/CT and CRT were significantly associated with improved survival times. A subgroup analysis showed no statistical difference in survival between the chemotherapy alone and CRT plus maintenance groups for those underwent CT examination (before PSM: 8 months vs 5 months, $p = 0.180$; and after PSM: 8 months vs 5 months, $p = 0.185$). However, for those underwent PET/CT examination, there was a significant difference between the aforementioned groups (before PSM: 25 months vs 11 months; and after PSM: 25 months vs 11 months, both, $p < 0.001$).

Table 1
Baseline characteristics of patients

BEFORE PSM			AFTER PSMa			
characteristics	No CRT (N=96)	CRT (N=96)	<i>P</i> value	No CRT (N=89)	CRT (N=89)	<i>P</i> value
Age(years)						
<60	46	47	0.885	46	40	0.368
≥60	50	49		43	49	
Gender						
Female	36	43	0.305	36	36	1
Male	60	53		53	53	
KPS						
<90	52	43	0.194	46	39	0.294
≥90	44	53		43	50	
Smoke						
No	55	58	0.660	50	51	0.880
Yes	41	38		39	38	
Pathological pattern						
SQC	35	37	0.766	35	36	0.878
Adenocarcinoma and others	61	59		54	53	
Position						
Central	62	56	0.374	55	53	0.759
Peripheral	34	40		34	36	
T classification						
T1-2	38	44	0.381	37	41	0.546
T3-4	58	52		52	48	

N, number of cases/controls; CRT, chest radiotherapy ; PSM, propensity score matching; a The PSM was performed using age and sex, which were subdivided according to the median values ;AD, adenocarcinoma.

BEFORE PSM			AFTER PSM ^a			
N classification						
N0-1	22	28	0.324	21	24	0.234
N2-3	74	68		68	65	
Image						
CT	46	52	0.386	44	49	0.453
PET/CT	50	44		45	40	
Weight loss						
≤5%	66	69	0.636	59	63	0.519
>5%	30	27		30	26	
Number of metastasis						
1	22	33	0.160	22	33	0.297
2	25	22		25	22	
3	19	14		19	11	
4	14	19		14	16	
5	16	8		9	7	
No. of metastatic organs						
1	47	55	0.144	47	55	0.454
2	32	33		32	27	
3	17	8		10	7	
Lung metastasis	47	50	0.665	44	44	1
Bone metastasis	46	44	0.772	39	37	0.762
Liver metastasis	13	9	0.365	8	9	0.799
Adrenal metastasis	7	3	0.194	6	3	0.305
Other metastasis	49	39	0.148	44	37	0.292
Mixed metastasis	48	41	0.311	41	34	0.288
N, number of cases/controls; CRT, chest radiotherapy ; PSM, propensity score matching; ^a The PSM was performed using age and sex, which were subdivided according to the median values ;AD, adenocarcinoma.						

Table 2
Univariate analysis between prognostic factors and overall survival(Before PSM)

characteristics	N	median survival time (months)	1-year os(%)	2-years os(%)	χ ²	P value
Age(years)						
<60	93	11	39.8	15.1	0.004	0.950
≥60	99	10	43.4	15.1		
Gender						
Female	79	11	44.3	20.3	2.382	0.123
Male	113	9	39.8	11.5		
KPS						
<90	95	9	35.8	12.6	1.383	0.240
≥90	97	12	47.4	17.5		
Smoke						
No	113	10	39.8	15.0	0.026	0.872
Yes	79	11	44.3	15.2		
Pathological pattern						
SQC	72	10	38.9	9.7	1.308	0.253
Adenocarcinoma and others	120	10	43.3	18.3		
Position						
Central	118	12	46.6	18.6	2.536	0.111
Peripheral	74	8	33.8	9.5		
T classification						
T1-2	82	12	48.8	19.5	3.819	0.051
T3-4	110	9	36.4	11.8		
N classification						
N0-1	50	15	56.0	24.0	7.560	0.006
N2-3	142	10	36.6	12.0		

N, number of cases/controls; PSM, propensity score matching.

characteristics	N	median survival time (months)	1-year os(%)	2-years os(%)	χ ²	<i>P</i> value
Image						
CT	98	6	25.3	2.0	58.629	<0.001
PET/CT	94	16	63.8	28.7		
Weight loss						
≤5%	135	11	43.7	12.6	0.204	0.651
>5%	57	10	36.8	21.1		
Chest radiotherapy						
No	96	8	32.2	6.3	13.118	<0.001
Yes	96	13	51.0	24.0		
Number of metastasis						
1	55	10	41.8	16.4	1.635	0.802
2	47	9	42.6	12.8		
3	33	12	45.5	12.1		
4	33	9	36.4	21.2		
5	24	11	41.7	12.5		
No. of matastatic organs						
1	102	10	42.2	14.7	0.289	0.865
2	65	11	41.5	16.9		
3	25	11	40.0	12.0		
Lung metastasis	97	11	45.4	17.5	1.499	0.221
Bone metastasis	90	11	38.9	16.7	0.021	0.884
Liver metastasis	22	9	36.4	13.6	0.340	0.560
Adrenal metastasis	10	5	40.0	0	4.143	0.042
Other metastasis	88	11	40.9	12.5	0.458	0.498
Mixed metastasis	89	11	41.6	15.7	0.026	0.871
N, number of cases/controls; PSM, propensity score matching.						

Table 3
Univariate analysis between prognostic factors and overall survival (After PSM)

characteristics	N	median survival time (months)	1-year os(%)	2-years os(%)	X2	P value
Age(years)						
<60	86	11	42.0	14.0	0.049	0.825
≥60	92	10	44.6	16.3		
Gender						
Female	72	11	44.4	19.4	1.716	0.190
Male	106	9	40.6	12.3		
KPS						
<90	85	9	36.5	12.9	0.857	0.355
≥90	93	12	47.3	17.2		
Smoke						
No	101	10	39.6	14.9	0.001	0.980
Yes	77	11	45.5	15.6		
Pathological pattern						
SQC	71	10	39.4	9.9	1.606	0.205
Adenocarcinoma and others	107	11	43.9	18.7		
Position						
Central	108	12	48.1	19.4	3.438	0.064
Peripheral	70	8	32.9	8.6		
T classification						
T1-2	78	12	50.0	19.2	3.623	0.057
T3-4	100	9	36.0	12.0		
N classification						
N0-1	45	15	55.6	22.2	6.026	0.014
N2-3	133	10	37.6	12.8		

N, number of cases/controls; PSM, propensity score matching.

characteristics	N	median survival time (months)	1-year os(%)	2-years os(%)	X2	P value
Image						
CT	93	7	21.5	2.2	52.554	<0.001
PET/CT	85	17	64.7	29.4		
Weight loss						
≤5%	122	11	44.3	12.3	0.240	0.624
≥5%	56	10	37.5	21.4		
Chest radiotherapy						
No	89	8	32.6	6.7	11.538	0.001
Yes	89	13	51.7	23.6		
Number of metastasis						
1	55	10	41.8	16.3	2.118	0.714
2	47	9	42.6	12.8		
3	30	11	43.3	10.0		
4	30	9	36.7	20.0		
5	16	12	50.0	18.8		
No. of matastatic organs						
1	102	10	42.2	14.7	0.092	0.955
2	59	11	40.7	15.3		
3	17	12	47.1	17.6		
Lung metastasis	88	11	45.5	17.0	0.872	0.350
Bone metastasis	76	11	39.5	17.1	<0.001	0.990
Liver metastasis	17	12	41.2	17.6	<0.001	0.991
Adrenal metastasis	9	5	44.4	0	2.713	0.100
Other metastasis	81	11	42.0	13.6	0.183	0.668
Mixed metastasis	75	11	42.7	16.0	<0.001	0.996
N, number of cases/controls; PSM, propensity score matching.						

3.4 Multifactorial analysis

Factors with significant differences in Univariate analysis were subjected to multifactorial analysis. In a multifactorial analysis (Table 4), patients who underwent PET/CT (before PSM: HR: 0.343, 95% CI: 0.250-0.471; and after PSM: HR: 0.348, 95% CI: 0.250-0.484, both $p < 0.001$) and CRT before PSM: HR: 0.624, 95% CI: 0.464-0.840, $p = 0.002$; and after PSM: HR: 0.630, 95% CI: 0.463-0.857, $p = 0.003$) had a more favorable prognosis than those who underwent CT and chemotherapy alone.

Table 4
Multivariate analysis between prognostic factors and overall survival

Before PSM				After PSM		
Factor	HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value HR
T classification (T1-2 vs. T3-4)	1.138	0.830- 1.561	0.422	1.127	0.811- 1.566	0.477
N classification(N0-1 vs. N2-3)	1.268	0.872- 1.843	0.214	1.278	0.861- 1.896	0.223
Image (CT vs. PET/CT)	0.343	0.250- 0.471	<0.001	0.348	0.250- 0.484	<0.001
Chest radiotherapy (NO CRT vs. CRT)	0.624	0.464- 0.840	0.002	0.630	0.463- 0.857	0.003

4. Discussion

Traditional NSCLC staging is based primarily on history, fiberoptic bronchoscopy, CT, magnetic resonance imaging, and other routine imaging examinations. If the lung cancer stage is inaccurate, an inappropriate treatment regimen will inevitably have an adverse impact on patient survival. PET/CT is an advanced diagnostic medical imaging technique that shows local metabolic function at a refined anatomical level, with a superior sensitivity and specificity than other examination methods, and allows a more effective detection of asymptomatic metastatic foci and metastatic lymph nodes [15]. Staging is more accurate when both metabolic function and anatomical information are assessed [16]. PET/CT can also improve the accuracy of depicting the target area for radiotherapy, avoiding missed target areas or increased exposure. Using PET/CT during an NSCLC radiotherapy program improves target volume delineation reliability and allows higher radiation doses without increasing side effect risks [17]. Accordingly, the volume of the scheduled irradiation target can be more accurately limited to morphologically and functionally defined tumor areas. Fewer normal tissues can be irradiated and higher total tumor doses can be used to seek optimal therapeutic effects and develop more rational treatments. Studies report that

occult extrathoracic metastases can be found in up to 37% of patients with advanced NSCLC, altering 14%-26% of NSCLC treatment decisions [18]. Although PET/CT benefits on NSCLC diagnosis have been widely reported, we compared the prognosis of patients who underwent PET/CT and CT and found that PET/CT-localized CRT improved survival, while CT imaging-guided radiotherapy did not, indicating a significant PET/CT advantage in extracranial oligometastatic NSCLC diagnosis. PET/CT has become the standard imaging tool for characterizing lung nodules [19], initial staging [20, 21], treatment planning, treatment response assessment [22], recurrence staging [23, 24], and lung cancer monitoring. The widespread clinical use of FDG-PET/CT in patients with lung cancer has improved staging and restaging accuracies, allowing for better treatment planning and treatment response assessments.

Local consolidation therapy is a common treatment for oligometastatic NSCLC. In 2016, Gomez et al. was the first to report the results of a phase II randomized trial that compared standard maintenance therapy (n=24) to local consolidation therapy (n=25) [25]. The median patient follow-up was 12.39 months, and the progression-free survival (PFS) was significantly better in the maintenance treatment group than in the local consolidation group (11.9 months vs. 3.9 months, $p=0.0054$). Adverse events were similar between both groups, with no treatment-induced grade 4 adverse events or deaths. Gomez et al. published the results of their latest long-term clinical study in 2019 and successfully confirmed that PFS (median, 14.2 months [95% CI, 7.4 to 23.1 months] with LCT vs. 4.4 months [95% CI, 2.2 to 8.3 months] with maintenance therapy or observation; $P=0.022$) and overall survival (median, 41.2 months [95% CI, 18.9 months to not reached] with LCT vs. 17.0 months [95% CI, 10.1 to 39.8 months] with maintenance therapy or observation; $P=0.017$) significantly improved by the early inclusion of LCT [26]. They also reported that both initial LCT before progression and delayed LCT after progression contributed to improved overall survival. In 2018, Iyengar et al. reported results from a phase II randomized trial comparing standard maintenance therapy with and without stereotactic ablative radiotherapy (SABR) in a patient population nearly identical to that of the trial reported by Gomez et al. and showed that PFS was significantly better in the SABR plus maintenance chemotherapy group than in the maintenance chemotherapy alone group (9.7 months vs. 3.5 months, $p=0.01$) [27]. Gomez et al. and Iyengar et al. both conducted phase II trials in patients with oligometastatic NSCLC to study the prognostic impact of aggressive local therapy. Both trials reported a significant increase in PFS by increasing aggressive local therapy. Moreover, our previous study showed that PET/CT-guided LCT was significantly efficient in patients with oligometastatic advanced lung cancer [7]. Overall survival rates were extremely higher in the LCT group than in the chemotherapy alone group (13 months vs. 7 months, $p=0.002$). Side effects incidence was similar between LCT and chemotherapy alone groups, and there were no treatment-related adverse outcomes or deaths. To explore more effective and personalized treatment options for oligometastatic lung cancer, we focused on evaluating the efficacy of extracranial oligometastases treated with CRT and revealed that similar efficacy was achieved with radiation therapy to the primary lung site alone compared to LCT, meaning that it is possible to achieve satisfactory outcomes with treatments that cause less damage to patients with extracranial oligometastatic NSCLC than maintenance treatments. There are several possible mechanisms that could explain the survival benefits of lung radiotherapy. First, after systemic treatment, hard-to-treat malignant cells, which are unlikely to be

eliminated by subsequent maintenance therapy and can serve as a source of following metastatic spread, are left behind. However, in such cases, CRT may reduce the number of such cells. Second, CRT may enhance the effects of systemic therapy by possibly making residual lesions more sensitive to subsequent maintenance therapy. A third possibility is that radiotherapy kills tumor cells by modulating the immune system. Radiotherapists are often subjective in the process of outlining tumor target areas based on CT images, and the influence of experience on the accuracy of tumor target area outlining can further affect the efficacy of radiotherapy. In particular, patients with advanced lung cancer often have complications such as pulmonary atelectasis, which is difficult to identify with the tumor lesions. Therefore, we believe that CT plays a limited role in the process of target area outlining, and it is difficult to improve the prognosis of lung cancer patients. A well-defined lesion is shown in PET/CT, which can exclude the influence of subjective factors on the accuracy of target area outlining and thus improve the efficacy of radiotherapy.

Immunotherapy was not included in this study because the patient information we analyzed was first obtained in 2013. As research progresses, it is increasingly recognized that there are complex interactions between radiotherapy and the immune system. In addition to producing a local therapeutic effect at the irradiated tumor site, radiotherapy can also cause spontaneous tumor regression in non-irradiated lesions; this is known as the abscopal effect [28]. Although the abscopal effect was studied for decades, the exact mechanism of this phenomenon is still unclear, and Demaria et al. [29] first linked the distal effect of radiotherapy to an immune-mediated mechanism. Preclinical studies suggest that radiotherapy is equivalent to an "agonist" in immunotherapy, making tumor cells more susceptible to T-cell-mediated immune attacks by modulating the immune system. Radiotherapy can enhance anti-tumor immune effects by inducing the release of more neoantigens from damaged tumor cells, enhancing the expression of major histocompatibility complex (MHC) class I molecules, and upregulating chemokines, cell adhesion molecules, and other immunomodulatory cell surface molecules, thereby inducing immunogenic cell death [30]. In terms of increasing attention to immunotherapy, the possibility of combining radiotherapy with immunotherapy is worth exploring, and this combination to produce synergistic antitumor activity shows great application prospects and development potential in the future.

5. Conclusions

PET/CT-guided chest radiation therapy is associated with improved clinical outcomes in patients with stage IV extracranial oligometastatic NSCLC. Advances in radiotherapy technology improved radiotherapy precision and ensured treatment safety, while improving radiotherapy effectiveness. Undoubtedly, the continuous optimization and innovation of radiotherapy technology in positioning, target area outlining, planning, and beam projection will continue to be a strong driving force for applying and developing radiotherapy in patients with lung cancer in the future. Future basic researches and large-sample randomized clinical trials on how to further optimize combinations of radiotherapy and systemic therapy, specifically in terms of targeted therapy and immunotherapy, in patients with lung cancer will be conducted.

Declarations

Author Contributions: Writing the original draft: TLW, CSL and YQS; formal analysis: CSL and YQS; data curation: TLW; software management: CYW; project administration: ZW; validation: GL; visualization: LH; draft review & editing: all authors; funding acquisition: TLW, YQS, additional resources: TLW.

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Institutional Review Board Statement: This statistical study was thoroughly reviewed and approved by the ethics committees of the First Hospital of China Medical University and the Liaoning Cancer Hospital. The whole research process was legal, reasonable, open, transparent, and strictly complied with the Declaration of Helsinki of 1964 and its later amendments or comparable ethical standards. The requirement for informed consent was waived due to the retrospective nature of this study.

Informed Consent Statement: The requirement for informed consent was waived due to the retrospective nature of this study.

Data Availability Statement: All data in this study are true and reliable.

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Figures

Figure 1

Flowchart depicting selection of the study population.

Figure 2

a.&b. Kaplan–Meier curve of overall survival for patients who did and did not receive PET/CT in the overall population (before PSM n=192,after PSM n=178).

c.&d. Kaplan–Meier curve of overall survival for patients who did and did not receive CRT in the overall population (before PSM n=192,after PSM n=178).

e.&f. Kaplan–Meier curve of overall survival for patients who did and did not receive CRT in the CT group(before PSM n=98,after PSM n=93).

g.&h. Kaplan–Meier curve of overall survival for patients who did and did not receive CRT in the PET/CT group(before PSM n=94,after PSM n=85).

Figure 3

a.&b. Subgroup analysis of OS among patients.

c.&d. Subgroup analysis of OS among patients in the CT group.

e.&f. Subgroup analysis of OS among patients in the PET/CT group.