RESEARCH

Locoregional progression-free survival of bone metastases from differentiated thyroid cancer

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Abstract

To evaluate the locoregional progression-free survival (LPFS) of bone metastatic lesions from differentiated thyroid cancer (DTC) after radioiodine therapy (RAIT) and to define its influencing factors, we performed a retrospective cohort analysis of 89 patients with bone metastases from DTC who received RAIT in our department over a 17-year period. The median follow-up time was calculated using the reverse Kaplan–Meier method. The log-rank test and a multivariate Cox proportional hazards regression model were performed in the analysis of prognostic indicators for LPFS. In this research, the median follow-up time for all patients was 47 (95% CI, 35.752–58.248) months, and that for patients with no progression was 42 months. The longest follow-up time was 109 months. The median LPFS time was 58 (95% CI, 32.602–83.398) months, and the 3- and 5-year LPFS probabilities were 57.8 and 45.1%, respectively. Multivariate analysis revealed bone structural changes as an independent risk factor for LPFS (P = 0.004; hazard ratio, 49.216; 95% CI, 3.558–680.704). Furthermore, the non–total-lesion uptake subgroup presented a worse LPFS than the total-lesion uptake subgroup in patients with structural bone lesions (P = 0.027). RAIT can improve the LPFS of radioiodine-avid bone metastases from DTC, especially those without bone structural changes.

Key Words

- differentiated thyroid cancer
- bone metastatic lesions
- radioiodine therapy
- locoregional progression-free survival
- bone structural changes

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Introduction

Bone metastasis is the second most common type of distant metastasis in differentiated thyroid cancer (DTC) after lung metastasis, with an incidence of 2–13%, strongly suggesting a poor prognosis (1, 2, 3, 4, 5, 6). Moreover, patients with bone involvements may experience skeletal-related events (SREs), which obviously threaten their mobility, ability to perform daily tasks, quality of life, and mental state (2, 7, 8, 9).

It has been hypothesized that early detection and appropriate treatment might improve the survival rate and quality of life of patients with DTC bone metastases (10). However, there is no standardized treatment regimen for these patients. At present, the main treatment modalities include surgery, radioiodine therapy (RAIT), external beam radiation therapy (EBRT), and bisphosphonate therapy (11). The American Thyroid Association noted that although radioiodine (I-131) is less likely to cure bone metastases, patients with positive I-131 uptake in bone lesions may still benefit from it (12). At present, studies of DTC patients with bone metastases treated with I-131 have focused on evaluating overall survival and have largely failed to assess the locoregional progression-free survival (LPFS) of bone foci. Given the negative impact of SREs on the quality of life, it is necessary to pay attention to the LPFS. In this

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study, the clinical characteristics of DTC bone metastases were described and analyzed so as to determine the factors affecting the control of LPFS in DTC bone lesions by RAIT.

Materials and methods

Patients

The medical records of 2781 patients with DTC treated with I-131 at the Department of Nuclear Medicine, Zhujiang Hospital of Southern Medical University, between January 2006 and December 2017 were reviewed, including 91 (3.3%) patients with bone metastases. Among these 91 patients, 1 female patient with single parietal bone metastasis and 1 male patient with single metastasis of the left eighth rib (histotypes: classic papillary thyroid carcinoma (PTC) and follicular variant of PTC, respectively) underwent resection of bone lesions before RAIT, so it was impossible to analyze the LPFS of bone lesions after RAIT in these cases. Therefore, 89 patients were included in the final analysis.

Definitions

The diagnostic criteria of bone metastasis were any of the following (13): (i) metastasis derived from DTC was confirmed by biopsy or postoperative pathology; (ii) bone lesions with I-131 uptake were classified as bone metastases if there were bone structural changes or a high value of serum thyroglobulin or thyroglobulin antibody; (iii) Finally, if the bone lesion was not confirmed by pathology or I-131 uptake, at least one imaging examination would need to yield positive results not explicable by other reasons.

The follow-up period was from the first RAIT after the diagnosis of bone metastasis to the date of the progression of bone lesions or the last follow-up.

The LPFS of bone foci after RAIT was defined as the time from the date of initial RAIT for bone metastases to the progression of bone lesions.

Bone metastasis locoregional progression was defined by the development of any of the following after initial RAIT: (i) new bone lesions or soft tissue components; (ii) new SREs (pathological fractures, cord compression, surgery, or EBRT) (13); (iii) Also, when a bone lesion was measurable (with a soft tissue mass ≥10 mm), an increase of at least 20% (with at least a 5-mm increase) in the diameter of the mass was considered progressive; on the contrary, when unmeasurable (no soft tissue mass or mass <10 mm), a substantial enlargement of the unmeasurable lesion was judged as unequivocal progression (14).

Bone structural changes include osteolysis, osteogenesis, and mixed bone destruction. The main manifestations of osteolytic lesions are patchy, punctured, and insect-etched osteolytic destruction, with irregular edges and disappearance of the bone cortex, but no surrounding osteosclerosis. Osteogenic lesions mainly exhibit nodular or sometimes ivory-like high density, with clear or unclear boundaries, complete bone cortex, and almost no change in bone contour (15).

RAIT

Our research team has previously described the implementation of RAIT and the collecting conditions of the post-therapy whole-body scans (16). Additional SPECT/CT images were performed immediately for suspected bone metastases with I-131 uptake, and CT or MRI examinations were performed within 1 month after RAIT to determine whether there were structural bone lesions.

Statistical analysis

Statistical analyses were conducted using the IBM SPSS Statistics 20.0 software (IBM Corporation). The Kaplan–Meier method was used to draw the LPFS curve of bone lesions after RAIT, and the reverse Kaplan–Meier method was used to calculate the median follow-up time of all patients. The log-rank test was used for univariate analysis to compare the differences in LPFS between two groups, and the Cox proportional hazards regression model was adopted for multivariate analysis. The hazard ratio (HR) and its 95% CI were reported. Bilateral $P < 0.05$ was statistically significant. The GraphPad Prism 8.0 software program (GraphPad Software) was used to create figures.

Ethics statement

This study was authorized by the local ethics committee (Medical Ethics Committee of Zhujiang Hospital of Southern Medical University) (batch no. 2020-KY-047-01) in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The need for informed consent was waived by the local ethics committee in view of the retrospective nature of the study.

Results

General characteristics

Thirty-one patients (34.8%) met all three diagnostic criteria (Fig. 1). The average age at diagnosis of bone metastases

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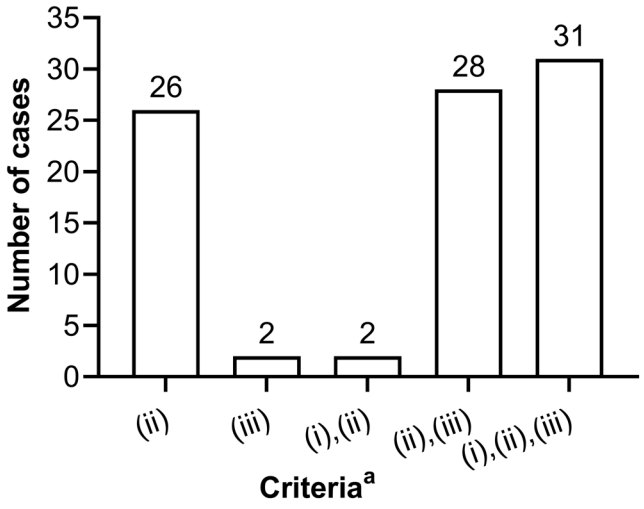

Figure 1
Diagnosis of DTC bone metastases. (A) Criteria: (i) metastasis derived from DTC was confirmed by biopsy or postoperative pathology; or (ii) Bone lesions with I-131 uptake were classified as bone metastases if there were bone structural changes or a high value of serum Tg or TgAb; (iii) Finally, if the bone lesion was not confirmed by pathology or I-131 uptake, at least one imaging examination would need to yield positive results not explicable by other reasons. DTC, differentiated thyroid cancer; I-131, radioiodine; Tg, thyroglobulin; TgAb, thyroglobulin antibody.

was 50.8 ± 12.8 years (Table 1), and the majority of patients were female (61.8%). The most common histotype of the primary tumor was follicular thyroid carcinoma (49.4%). Fifty-seven patients showed other distant metastases when bone lesions were treated with I-131 for the first time, with lung metastasis being the most common type (56/57).

Characteristics of bone metastases

In this cohort of 89 patients, a total of 36 people developed SREs, among whom 9 developed SREs before and after initial RAIT for bone metastases, 19 (52.8%) developed SREs only before initial RAIT, and 8 (22.2%) developed SREs only after initial RAIT. Twenty-eight patients (31.5%) developed SREs before initial RAIT, among whom 20 had more than one type of SRE (Table 2). Thirty-one patients (34.8%) had bone metastasis as the initial symptom of primary thyroid cancer (Table 1). Soft tissue masses were observed in 35 patients (39.3%). Twenty-five patients (28.1%) had no bone structural changes. Seventy (78.7%) patients had I-131 uptake in all bone lesions. The majority of patients (79.8%) had multiple bone lesions. A total of 457 bone lesions were found among 89 patients (Table 3).

All patients received RAIT, among whom 33 received other treatments prior to initial RAIT for bone metastases; of these, 24 underwent surgery only, 2 received EBRT only, and the remaining 7 received at least two types of other treatments (Table 4). The operation sites of 18 patients were located in the spine. Eleven patients (12.4%) received postoperative RAIT prior to the diagnosis of bone metastasis, 50 (56.2%) underwent their first RAIT following the diagnosis of bone metastasis, and the remaining 28 (31.5%) were diagnosed with bone metastasis during the first RAIT.

LPFS of bone metastatic lesions after initial RAIT

The median follow-up time of all patients was 47 months (95% CI, 35.752–58.248 months), whereas that of patients without progression was 42 months, and the longest follow-up time was 109 months (~9.1 years). Forty-two (42/89) patients experienced progression, as seen in Table 1, and the most common manifestation was new bone lesions (28 cases), followed by new SREs (6 cases), enlargement in measurable soft tissue masses (6 cases), and new soft tissue masses (2 cases).

The median LPFS time of bone lesions after initial RAIT of all patients was 58 months (95% CI, 32.602–83.398 months), and the 3- and 5-year LPFS probabilities were 57.8 and 45.1%, respectively (Fig. 2). Log-rank analysis (Fig. 3 and Table 5) showed that the impacts of the following six variables on LPFS were statistically significant: bone metastasis as the initial symptom ($P < 0.001$), receiving other treatments before initial RAIT ($P < 0.024$), the occurrence of SREs before initial RAIT ($P = 0.046$), the extent of I-131 uptake of bone lesions ($P < 0.001$), with or without bone structural changes ($P < 0.001$) and bone metastases with or without soft tissue components ($P < 0.001$). Multivariate analysis showed that changes in bone structure were an independent risk factor for LPFS ($P = 0.004$; HR, 49.216; 95% CI, 3.558–680.704). Compared to those without bone structural changes, patients with bone structural changes had a 49.2-fold higher risk of progression after RAIT. According to I-131 uptake of structural bone lesions, patients with bone structural changes were further divided into two subgroups (total-lesion and non–total-lesion uptake, respectively) for analysis. There was a statistically significant difference in LPFS between the total- and non–total-lesion uptake subgroups ($P=0.027$, Fig. 4), and involvement in the non–total-lesion uptake subgroup was associated with worse LPFS. Furthermore, additional analyses of patients with I-131 uptake in all bone lesions were performed, and the results were similar to those of the overall study group. Bone metastasis as the initial symptom ($P < 0.001$), other treatments ($P=0.008$), SREs ($P=0.015$),

Table 1 Basic information of DTC cases with bone metastases (n = 89).

Characteristics	Number of patients (%)
Age at diagnosis (years)	50.81 ± 12.771, range: 21–79
<55	54 (60.7)
Gender	
Female	55 (61.8)
Histotypes of primary focus	
Classic PTC	25 (28.1)
Follicular PTC	15 (16.9)
FTC	44 (49.4)
Mixed (PTC + FTC)	3 (3.4)
Unknown	2 (2.2)
Non-bone distant metastases	57 (64.0)
Lung	47 (52.8)
Brain	1 (1.1)
Lung and liver	5 (5.6)
Lung and kidney	1 (1.1)
Lung and adrenal	1 (1.1)
Lung, liver and kidney	2 (2.2)
Bone metastasis as initial symptom	31 (34.8)
Other treatments before initial RAIT	33 (37.1)
SREs before initial RAIT	28 (31.5)
Multiple bone metastasis	71 (79.8)
Degrees of I-131 uptake of bone metastases:	
All bone lesions with uptake	70 (78.7)
Some bone lesions with uptake	17 (19.1)
No uptake	2 (2.2)
Bone structural changes	
Osteolysis	39 (43.8)
Osteogenesis	4 (4.5)
Mixed	21 (23.6)
No	25 (28.1)
Soft tissue mass	35 (39.3)
Progression of bone metastasis	42 (47.2)
Types of progression (n = 42)	
New bone lesions	28 (66.7)
Enlargement in mearurable soft tissue masses	6 (14.3)
New SREs	6 (14.3)
New soft tissue masses	2 (4.8)
Median number of RAIT coursese	2, range: 1–11
Single average I-131 activity	
Unknown	4
Median (GBq)	7.5, range: 4.0–9.6
Cumulated I-131 activity	
Unknown	4
Median (GBq)	15.7, range: 4.4–92.1

DTC, differentiated thyroid cancer; FTC, follicular thyroid carcinoma; I-131, radioiodine; PTC, papillary thyroid carcinoma; RAIT, radioiodine therapy; SREs, skeletal-related events; Tg, thyroglobulin.

bone structural changes (P < 0.001), and soft tissue masses (P < 0.001) were statistically correlated with LPFS in log-rank analysis, but only structural changes independently affected LPFS after multivariate analysis (P = 0.013; HR, 58.117; 95% CI, 2.339–1444.100).

Table 2 Types of SREs before initial RAIT for bone metastases.

Types of SREs	Number of patients (n = 28)
Surgery	6
Surgery, pathological fractures	2
Surgery, cord compression	8
Surgery, EBRT	1
Surgery, intra-operative EBRT	1
Surgery, pathological fractures, cord compression	2
Surgery, cord compression, EBRT	1
Surgery, pathological fractures, cord compression, EBRT	2
Pathological fractures	1
pathological fractures, cord compression	1
EBRT	2
EBRT, cord compression	1

EBRT, external beam radiation therapy; RAIT, radioiodine therapy; SREs, skeletal-related events.

Discussion

A prior review mentioned that bone metastases occurred in 2–13% of DTC patients (6), and our study observed a rate of 3.3% (91/2781), consistent with the findings of the aforementioned review. The total incidence of SREs in this cohort was 40.4% (36/89), which was lower than that of 78% (192/245) reported by Farooki *et al.* (1). This discrepancy may be related to the fact that the subjects of their study were from the Memorial Sloan Kettering Cancer Center, which focuses on multidisciplinary treatment of advanced thyroid cancer, so a referral bias might have overestimated the rates of SREs if patients who did not experience SREs were unlikely to be referred to the center. It is undeniable that the incidence of SREs in DTC bone metastasis is high. In view of the serious threat to the quality of life caused by

Table 3 Distributions of bone lesions.

Sites of metastases	Number of bone lesions (n = 457)	%
Skull	43	9.4
Clavicle	7	1.5
Sternum	21	4.6
Shoulder blade	14	3.1
Rib	85	18.6
Cervical vertebra	25	5.5
Thoracic vertebra	77	16.8
Lumbar vertebra	40	8.8
Sacral vertebra	27	5.9
Upper limb	12	2.6
Lower limb	20	4.4
Pelvis	86	18.8

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Table 4 Details of additional treatments prior to initial RAIT for bone metastases (n = 33).

Patients	Treatment	Sites of surgery (ablation or open resection)	Contents of surgery
1	EBRT	–	–
2	EBRT	–	–
3	EBRT, chemotherapy	–	–
4	Surgery	Iliac crest	Ablation resection + iliac crest internal fixation
5	Surgery, EBRT	Sacral vertebra	Ablation resection + intra-operative EBRT
6	Surgery	Iliac crest	Open resection
7	Surgery	Thoracic vertebra	Open resection + internal spine fixation
8	Surgery	Temporal bone	Open resection
9	Surgery	Thoracic vertebra	Open resection + internal spine fixation
10	Surgery	Iliac crest	Open resection
11	Surgery	Sacral vertebra	Open resection + internal spine fixation
12	Surgery	Thoracic vertebra	Open resection + internal spine fixation
13	Surgery	Cervical vertebra, thoracic vertebra	Open resection + internal spine fixation
14	Surgery	Cervical vertebra	Open resection + internal spine fixation
15	Surgery	Lumbar vertebra	Open resection + internal spine fixation
16	Surgery	Iliac crest	Open resection
17	Surgery	Thoracic vertebra	Open resection + internal spine fixation
18	Surgery	Skull	Open resection
19	Surgery	Thoracic vertebra	Open resection + internal spine fixation
20	Surgery	Sternum	Open resection
21	Surgery	Mandible	Open resection
22	Surgery	Thoracic vertebra, lumbar vertebra	Open resection + internal spine fixation
23	Surgery	Sternum	Open resection
24	Surgery	Parietal, cervical vertebra	Open resection of lesion of the parietal (not of the cervical vertebra) + internal spine fixation
25	Surgery	Humerus	Open resection + internal humerus fixation
26	Surgery	Thoracic vertebra	Open resection + internal spine fixation
27	Surgery	Thoracic vertebra	Open resection + internal spine fixation
28	Surgery, EBRT	Thoracic vertebra	Open resection + internal spine fixation
29	Surgery, EBRT	Lumbar vertebra	Open resection + internal spine fixation
30	Surgery, EBRT	Lumbar vertebra	Open resection + internal spine fixation
31	Surgery, EBRT	Thoracic vertebra	Open resection + internal spine fixation
32	Surgery, EBRT, chemotherapy	Thoracic vertebra	Open resection + internal spine fixation
33	Surgery	Parietal, ischium	Open resection + ablation resection

EBRT, external beam radiation therapy; RAIT, radioiodine therapy.

SREs, the importance of improving the evaluation, timely detection, and prevention of SREs is emphasized.

This study analyzed 11 factors that may affect the efficacy of RAIT in DTC bone lesions. The univariate analysis suggested that five factors – bone metastasis as the initial symptom of primary focus, receiving other treatments before initial RAIT, the occurrence of SREs before initial RAIT, not all bone lesions with I-131 uptake, and bone lesions with soft tissue masses – were associated with poorer LPFS but could not be transformed into a shorter LPFS time with statistical differences in multivariate analysis, so they cannot serve as independent predictors. The reason for this might be because this was a single-center study with a small sample size of only 89 cases. The findings of this study will need to be confirmed by a multi-center study with a large sample size.

Because there is a lack of relevant literature on the LPFS of bone lesions after RAIT, and many studies about bone metastasis have been conducted in cohorts of subjects with distant metastasis rather than DTC bone metastasis, this topic is discussed below by drawing lessons from studies associated with distant metastasis, responses to efficacy, and survival.

The 2015 edition of the American Thyroid Association guidelines indicate that although RAIT for bone metastases is rarely curative, those with I-131–avid lesions may still benefit from it (12). To date, many studies have focused on the impact of I-131 uptake on survival, and all suggest that the prognosis of patients with I-131–avid bone lesions is better. In a retrospective study (17), 43% of 295 patients with I-131–avid distant metastases from DTC showed negative results on imaging (both I-131 whole-

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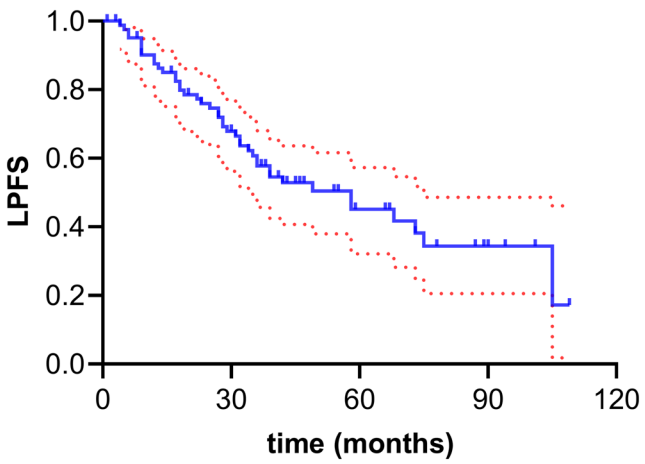

Figure 2
LPFS curve and its 95% CI of bone lesions after initial RAIT of all patients. LPFS, locoregional progression-free survival; RAIT, radioiodine therapy.

body scan and standard radiograph) after treatment. The rate of recurrence was only 7% for those who achieved negative imaging, and their 10-year overall survival rate after RAIT was 92% compared to 29% for those who did not. In addition, the research reported that the 10- and 15-year metastatic survival rates of patients with positive I-131 uptake in DTC distant metastases were 56% and 45%, whereas those without uptake decreased significantly to 10% and 6%, respectively (17). In the study by Kondraciuk *et al.* (11), 27 patients with bone metastases from thyroid cancer had I-131 uptake and 14 did not. After univariate analysis in this subgroup, it was found that those with uptake had better survival outcomes than those without uptake (3-year metastatic survival rate: 96% vs 54%, $P=0.01$). Petrich *et al.* reported that the average survival time of DTC patients with I-131–avid bone lesions was 8.9 years, which was significantly longer than that of those without uptake (average, 1.2 years after diagnosis) ($P < 0.005$) (18).

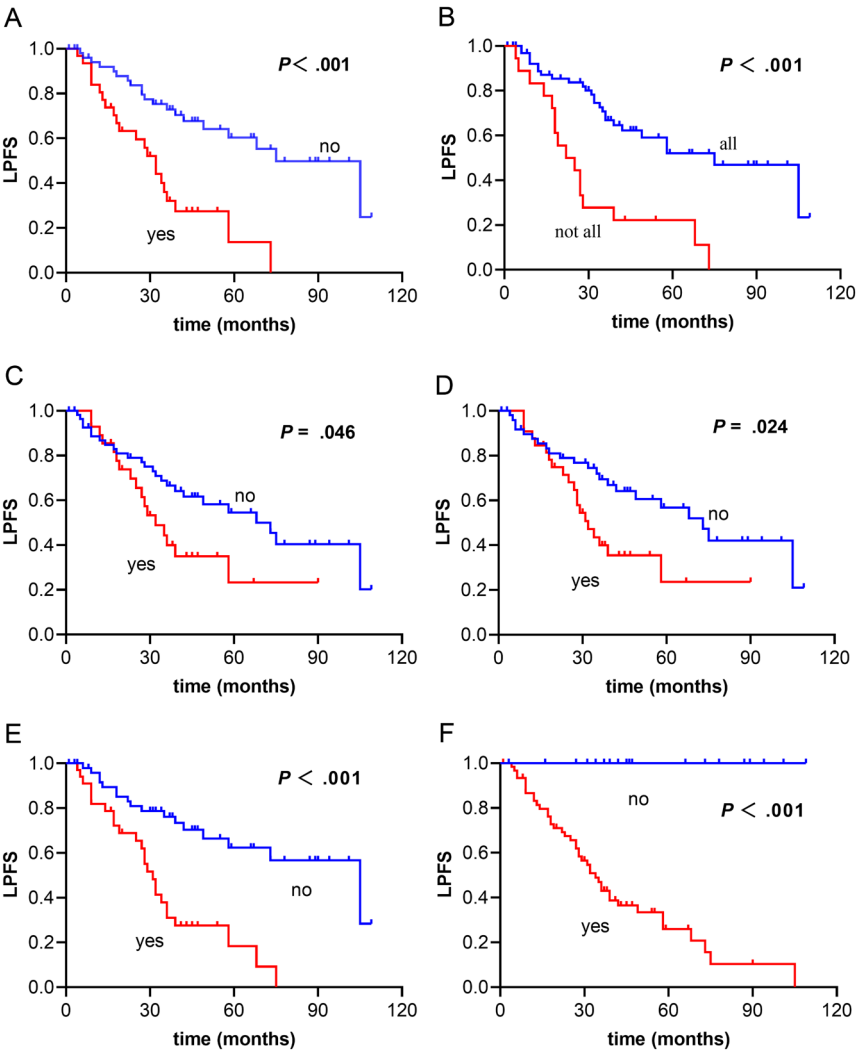

Figure 3
LPFS curves of the variables with log-rank $P < 0.05$. (A) Bone metastasis as the initial symptom. (B) Extent of I-131 uptake of bone lesions. (C) SREs before initial RAIT. (D) Other treatments before initial RAIT. (E) Soft tissue masses. (F) Bone structural changes. I-131, radioiodine; LPFS, locoregional progression-free survival; RAIT, radioiodine therapy; SREs, skeletal-related events.

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Table 5 Univariate and multivariate analysis of the factors associated with the LPFS of bone lesions after initial RAIT.

Characteristics	Total (n = 89) (%)	Progression (n = 42)	Median LPFS (months)	Log-rank		Cox proportional risk regression model	
				χ^2	P	P	HR (95% CI)
Age at diagnosis (years)							
<55	54 (60.7)	26	58	0.101	0.751		
≥55	35 (39.3)	16	49				
Gender							
Male	34 (38.2)	17	32	2.249	0.134		
Female	55 (61.8)	25	68				
Histotypes of primary focus							
PTC	40 (44.9)	17	73	0.462	0.497		
Not PTC	47 (52.8)	24	42				
Unknown	2 (2.2)	1	–				
Non-bone distant metastases							
Yes	57 (64.0)	27	58	0.001	0.977		
No	32 (36.0)	15	58				
Bone metastasis as initial symptom							
Yes	31 (34.8)	22	32	15.397	<0.001	NS	–
No	58 (65.2)	20	75				
Other treatments before initial RAIT							
Yes	33 (37.1)	22	32	5.121	0.024	NS	–
No	56 (62.9)	20	73				
SREs before initial RAIT							
Yes	28 (31.5)	17	32	3.995	0.046	NS	–
No	61 (68.5)	25	68				
Number of bone metastasis							
Solitary	18 (20.2)	6	75	2.256	0.133		
Multiple	71 (79.8)	36	39				
Degree of I-131 uptake							
All	70 (78.7)	26	75	17.612	<0.001	NS	–
Not all	19 (21.3)	16	22				
Bone structural changes							
Yes	64 (71.9)	42	28.5	27.235	<0.001	0.004	49.216 (3.558–680.704)
No	25 (28.1)	0	–				
Soft tissue mass							
Yes	35 (39.3)	25	31	18.305	<0.001	NS	–
No	54 (60.7)	17	105				

I-131, radioiodine; HR, hazard ratio; LPFS, locoregional progression-free survival; NS, not significant; PTC, papillary thyroid carcinoma; RAIT, radioiodine therapy; SREs, skeletal-related events.

Similarly, Pittas *et al.* found that the presence of I-131–avid bone lesions was an independent favorable prognostic indicator for survival (4). It was suggested that patients with I-131–avid bone lesions should be treated with I-131 to prolong their survival time and improve their prognosis. However, the above studies did not further analyze the degree of I-131 uptake to explore its impacts on survival or progression-free survival.

It was observed in the present study that positive I-131 uptake was also helpful for improving the LPFS of structural bone lesions after RAIT. There were too few patients without uptake in any bone lesions in the cohort (only two cases), so all patients were divided into two groups in the statistical analysis, that is, those with all bone lesions with uptake and those with not all bone lesions with uptake, respectively. The univariate analysis showed that

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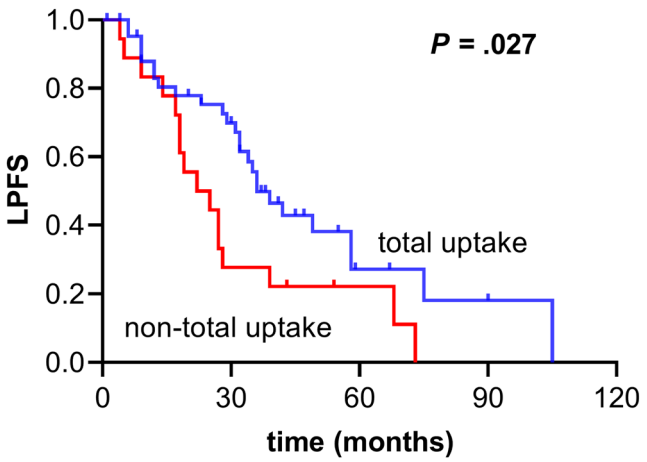

Figure 4
LPFS curves for total- and non–total-lesion uptake subgroups in patients with bone structural changes. LPFS, locoregional progression-free survival.

there was a difference in the LPFS between the two groups ($P < 0.001$), but no statistical difference was obtained after the Cox regression analysis. However, after the subanalysis in patients with bone structural changes, the total-lesion uptake subgroup showed a better LPFS than the non–total-lesion uptake subgroup. It is suggested that the LPFS of structural bone metastases with good uptake is longer than that with poor uptake.

Patients with DTC bone metastases with I-131 uptake but no bone structural changes generally have a good prognosis after RAIT. In the present study, the presence of structural bone lesions was an independent predictor of poor prognosis in LPFS. Robenshtok *et al.* included 14 patients with bone metastases of thyroid cancer who had no structural changes in CT or MRI but exhibited I-131 uptake for retrospective analysis (19); after a median follow-up of 5 years (range, 2–14 years), all patients survived, and none had experienced bone structural changes or SREs, suggesting that I-131–avid bone metastases without structural lesions could be resolved after RAIT without causing SREs. Hindie *et al.* observed that six out of eight patients with bone metastases without structural changes found for the first time by I-131 scans went into complete remission after RAIT and did not require additional treatment (20). Petrich *et al.* also observed several patients with DTC bone metastases with a small number (≤3) of bone lesions, whose bone metastases with negative anatomical imaging examination but positive I-131 uptake were relieved after treatment (18). When bone metastases do not cause structural changes on imaging, it indicates that the disease is in the early stage. When I-131 whole-body scintigraphy shows positive I-131 uptake in the bone lesions, it suggests that the tumor is well differentiated. Such functional lesions may achieve complete remission after RAIT, so their LPFS can be prolonged. However, when structural changes occur, it suggests that the course of the disease is longer and some lesions may be de-differentiated, which makes them less sensitive to I-131, rendering the treatment less effective.

This is a single-center and retrospective study, which may have led to a selection bias, and the inherent limitation of a retrospective study is that the relationship between research factors and conclusions is exploratory. Notably, this study is the first to assess the LPFS of bone metastasis after RAIT. Moreover, considering the low incidence of DTC bone metastasis, it is difficult to conduct a prospective study, and the sample size included in this study is relatively large, which may decrease the bias to some extent.

Conclusions

Bone metastases with structural changes but good I-131 uptake correlate with good LPFS after RAIT, while I-131–avid bone lesions without structural changes independently predict a better prognosis, indicating that RAIT can be actively applied to these bone lesions to prolong the LPFS time and improve the quality of life of DTC patients.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement
Huijuan Feng and Wei Ouyang conceived the study. Jiaxin Luo, Weili Yin, and Qiuxia Lin designed the study. Data collection were performed by Liqin Pan and Yanying Chen. Data analysis was performed by Jing Wang and Zhen Li. Jiaxin Luo, Juqing Wu, Pan Chen, and Yuanna Ling discussed the results. The initial draft was written by Jiaxin Luo, Weili Yin, and Qiuxia Lin. Huijuan Feng and Wei Ouyang revised it critically for important intellectual content. All authors commented on previous versions of the manuscript, as well as read and approved the final manuscript.

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