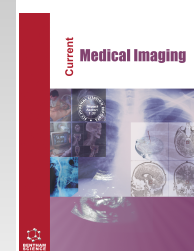




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RESEARCH ARTICLE

Effects of Iodinated Contrast-enhanced CT on Urinary Iodine Levels in Postoperative Patients with Differentiated Thyroid Cancer

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Abstract:

Aims:

This study aims to observe the fluctuating urine iodine levels in patients with differentiated thyroid cancer (DTC) following iodinated contrast-enhanced computed tomography (eCT) scans.

Background:

The presence of iodine in iodinated contrast agents (ICAs) can impede the effectiveness of radioactive iodine treatment (RAIT) and diagnostic scans in individuals diagnosed with DTC, as it can engage in competitive interactions with ¹³¹I. According to established guidelines, it is recommended to postpone RAIT for a period of three to four months in individuals who have had prior exposure to ICAs. The measurement of spot urine iodine concentration is a valuable indicator for assessing the overall iodine content throughout the body.

Objective:

The objective is to identify the optimal timing for administering postoperative RAIT in DTC patients.

Methods:

At various time points after surgery, a cohort of 467 random urine samples (126 male samples, 341 female samples, age (45±12 years)) was obtained from 269 DTC patients. The samples were analyzed for urinary iodine and urinary creatinine levels, and the urinary iodine/urine creatinine ratio (I/Cr) was computed. All samples were divided into two groups according to whether eCT before operation: the non-enhanced CT (eCT-) group and the enhanced CT (eCT+) group. The urine samples in the eCT- group were categorized into four subgroups according to the duration of strict low iodine diet (LID): (eCT-I+) no LID; (eCT-I-2W) 2 weeks of LID; (eCT-I-4W) 4 weeks of LID; and (eCT-I-6W) 6 weeks of LID. The last three groups were merged into the eCT- and effective LID group (eCT- I-). The urine samples from the eCT+ group were categorized into five subgroups: (0.5M eCT+) 0.5 month after eCT+; (1M eCT+) 1 month after eCT+; (2M eCT+) 2 months after eCT+; (3M eCT+) 3 months after eCT+; (≥4M eCT+) ≥4 months after eCT+. In addition, the patients within 2 months after eCT+ were divided into 2 groups according to their LID: no effective LID group (eCT+ I-) and effective LID group (eCT+ I-). Utilizing the Kruskal-Wallis and Mann-Whitney U rank sum tests, the differences in I/Cr between groups were compared.

Results:

In the eCT-group, the I/Cr ratios of eCT-I-2W, eCT-I-4W, and eCT-I-6W were significantly lower than those of eCT-I+ (χ^2 values: 4.607.99, all $P < 0.05$). However, there was no significant difference in I/Cr between eCT-I-2W, eCT-I-4W, and eCT-I-6W (2 values: 0.591.31, all $P > 0.05$). Significantly higher I/Cr values were observed in 0.5M eCT+ and 1M eCT+ than in eCT-I+ (χ^2 values: 3.22 and 2.18, respectively, all $P < 0.05$). There was no significant difference in I/Cr between 2M eCT+ and eCT-I+ ($\chi^2 = 0.76$, $P = 0.447$). The I/Cr ratios of 3M eCT+, ≥4M eCT+ were not significantly different with eCT-I- (χ^2 values: 1.76; 0.58; all $P > 0.05$). However, they were considerably lower than eCT-I+ (χ^2 values: 7.03; 5.22; all $P < 0.05$). The I/Cr for patients who underwent eCT within two months (eCT+ I-, eCT+ I+) did not differ significantly ($\chi^2 = 1.79$, $P = 0.073$).

Conclusion:

For patients who are considering receiving radioactive iodine therapy (RAIT) following a diagnosis of differentiated thyroid cancer (DTC), it is recommended that the interval between RAIT treatment and enhanced computed tomography [eCT] scans be conducted at least three months.

Keywords: Differentiated thyroid cancer, Iodinated contrast, Enhanced CT, Urinary iodine level, Radioactive iodine therapy, CT scans.

Article History

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1. INTRODUCTION

Thyroid cancer is widely recognized as the prevailing carcinoma of the endocrine system and has emerged as the malignancy with the greatest incidence among females in some nations [1, 2]. The primary pathological classifications of thyroid cancer are papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma, and anaplastic thyroid carcinoma. The aforementioned two conditions are referred to as differentiated thyroid cancer (DTC). The majority of thyroid carcinomas, namely over 90%, are classified as differentiated thyroid carcinomas (DTC). Among DTCs, around 80% are identified as papillary thyroid carcinomas, whereas follicular carcinoma comprises 11% of cases. The primary therapeutic modality employed for the management of thyroid cancer is surgical intervention. Postoperative thyroid-stimulating hormone (TSH) suppression therapy and ¹³¹I radioiodine therapy (RAIT) are the primary adjunctive interventions utilized in the management of differentiated thyroid cancer (DTC). Radiation therapy (RAIT) has been shown to be successful in reducing the likelihood of recurrence and increasing the duration of disease-free life in patients who are at a high risk of recurrence following differentiated thyroid cancer (DTC) [3, 4]. Nevertheless, it is important to note that there exists a competitive interaction between stable iodine and radioactive iodine within the body. This interaction hinders the entry of radioactive iodine into residual thyroid and DTC metastases. Consequently, in order to ensure the desired therapeutic outcome, it is imperative to adhere to a strict low iodine diet (LID) prior to receiving radioactive iodine therapy (RAIT) in order to reduce the iodine levels within the body [5, 6]. Neck iodinated enhanced CT (eCT) has demonstrated its ability to effectively assess cervical lymph node metastasis in certain patients with differentiated thyroid cancer (DTC). This evaluation can provide valuable guidance in developing personalized surgical plans, particularly in cases where the tumor is of significant size and involves the invasion of tracheal, esophageal, and mediastinal lymph nodes [7, 8]. Iodinated contrast is commonly administered to improve the diagnostic efficacy of computed tomography (CT). The administration of contrast material leads to a significant augmentation in the accumulation of iodine within the body, which is a process and it is gradually eliminated over a period of many weeks to months. A standard computed tomography (CT) scan typically employs around 100 cc of intravenous contrast material, corresponding to approximately 30 g of iodine. There is worry that this temporary rise in iodine can compete with ¹³¹I and interfere with later care, such as whole-body scans and therapy with radioactive iodine in thyroid cancer patients. Furthermore, several organizations advocate for the use of iodine depletion diets as a means to enhance the therapeutic efficacy of radioactive iodine in individuals with this condition. Therefore, it is crucial to avoid the use of iodinated contrast material due to its potential to diminish the efficacy of radioactive treatment. Nevertheless, it is crucial to consider the impact of the iodine

contrast medium on radioiodine ablation therapy (RAIT) following enhanced computed tomography (eCT) due to the substantial presence of iodine in the contrast medium and its prolonged retention in the patient's body. This problem holds significant clinical relevance. Several retrospective investigations have indicated that the iodine levels in patients can decrease to a level that does not impact the therapeutic efficacy of ¹³¹I iodine after a period of 1-4 months of improved CT [3, 4, 9]. Nevertheless, there is a lack of documentation about the fluctuating patterns of urine iodine levels subsequent to the administration of iodinated contrast agents. This study aimed to assess the temporal variations in urinary iodine levels following enhanced computed tomography (eCT) using an iodinated contrast medium. The objective was to provide a framework for identifying the optimal time gap between postoperative procedures and radioactive iodine therapy (RAIT) in patients with differentiated thyroid cancer (DTC) who had undergone eCT.

2. MATERIALS AND METHODS

Urine samples were collected from patients who came to the Department of Nuclear Medicine, Hangzhou Cancer Hospital, and the clinical data of the patients were collected, including gender, age, LID, whether eCT was performed, and the time interval between eCT and urine retention. This study was approved by the hospital Ethics Committee. The patients to be treated with RAIT were given strict guidance of LID before treatment, and iodine-containing foods (mainly iodized salt and seafood) and medicines were avoided [10].

All patients underwent total thyroidectomy. Patients who underwent CT scans were injected with a water-soluble iodine contrast agent. Patients with impaired renal function (serum creatinine <4 $\mu\text{mol/L}$ or >73 $\mu\text{mol/L}$) were excluded. Two urine samples (about 20 ml/tube) were taken from each patient for the determination of urinary iodine and creatinine levels. Urinary iodine was determined within 7 days after urine retention based on the principle of iodine-catalyzed arsenic-cerium reaction. The kit was provided by Wuhan (Hubei, China) Zhongsheng Biochemical Technology Co., Ltd., and the detection range was 10-400 $\mu\text{g/L}$. Urine creatinine was routinely tested in the clinical laboratory. The ratio of urine iodine/urine creatinine (I/Cr) ($\mu\text{g/gCr}$) was calculated.

All samples were divided into two groups according to whether eCT before operation: the non-enhanced CT (eCT-) group and the enhanced CT (eCT+) group. The eCT- group was further divided into four subgroups according to the duration of LID: a) no LID group (eCT- I-); b) 2 weeks of LID group (eCT- I- 2W); c) 4 weeks of LID group (eCT- I- 4W); d) ≥ 6 weeks of LID group (eCT- I- $\geq 6\text{W}$). The eCT+ group was further divided into five subgroups according to the time interval between eCT examination and urinary iodine measurement: a) 0.5 month after eCT+ group (0.5M eCT+); b) 1 month after eCT+ group (1M eCT+); c) 2 months after the eCT+ group (2M eCT+); d) 3 months after the eCT+ (3M eCT+); e) ≥ 4 months after eCT+ group ($\geq 4\text{M}$ eCT+). There was more than 2 weeks for LID in both 3M eCT+ and $\geq 4\text{M}$ eCT+ groups. The scheme of groups and subgroups is shown in Fig. (1).

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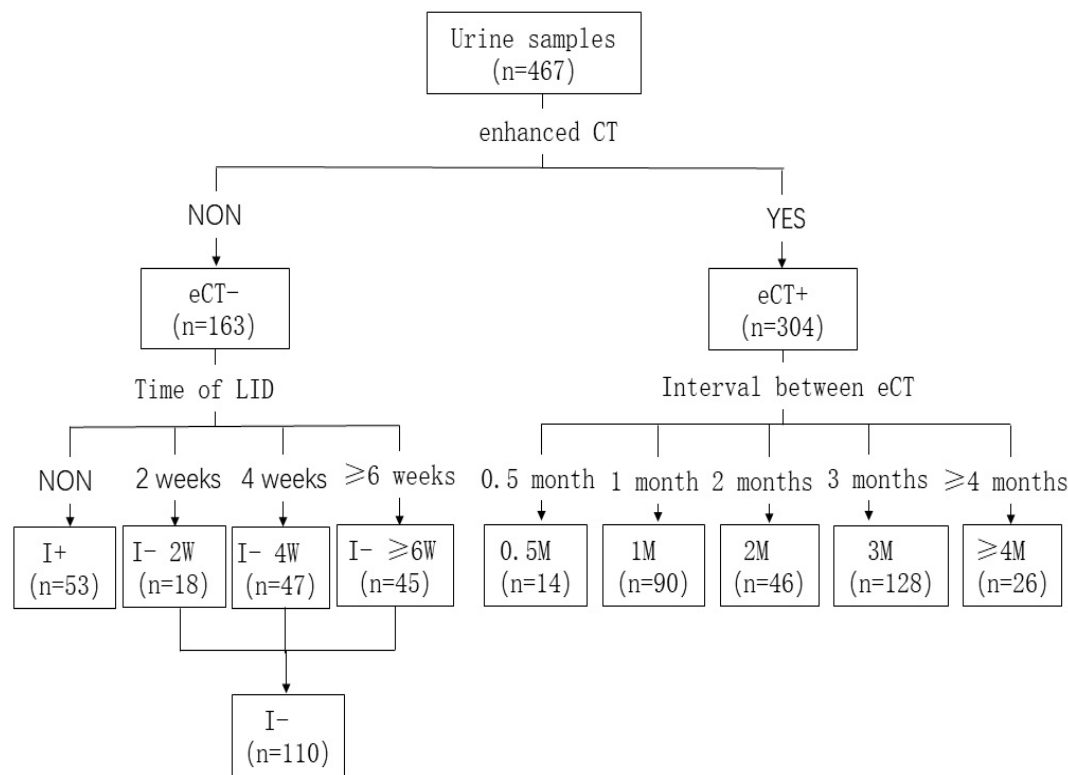


Fig. (1). The scheme of groups and subgroups. **I+:** No LID group; **I- 2W:** 2 weeks of LID group; **I- 4W:** 4 weeks of LID group; **I-≥6W:** ≥ 6 weeks of LID group. **I-:** The data were collected from **I- 2W**, **I- 4W** and **I-≥6W**. **0.5M:** 0.5 month after eCT+; **1M:** 1 month after eCT+; **2M:** 2 months after the eCT+; **3M:** 3 months after the eCT+; **≥4M:** ≥4 months after eCT+

Table 1. Patients’ baseline characteristics.

Characteristics	Value	P-value
Age of patients (years)	45 ±12 years	-
-	-	-
Patients type [n (%)]		-
Patients with DTC	269, 58 %	0.102
Patients with no DTC	198, 42 %	
Gender [n (%)]	-	-
Male	126, 27 %	0.0215
Female	341, 73 %	
Total urine sample	467, 100 %	-
Category of urine sample [n, %]	-	-
Enhanced CT group (eCT ⁺)	304, 66%	0.004
Non-enhanced CT group (eCT ⁻)	163, 34%	
Non-enhanced CT group [n (%)]	163	-
Level of I/Cr (µg/gCr)	-	-
I/Cr = 106.86	53, 33 %	0.035
I/Cr = 42.50	18, 11%	
I/Cr = 34.96	47, 29 %	
I/Cr = 27.07	45, 27 %	
Enhanced CT group [n (%)]	304	-
Level of I/Cr (µg/gCr)	-	-

(Table 1) contd.....

Characteristics	Value	P-value
I/Cr = 425.06	14, 5 %	0.638
I/Cr = 157.34	90, 29 %	
I/Cr = 91.19	46, 15 %	
I/Cr = 39.79	128, 42 %	
I/Cr = 37.76	26, 9 %	-

Due to the high level of iodine in the body after eCT, LID did not reduce the level of iodine in the body to the normal level in a short time. So we retrospectively divided the patients within 2 months after eCT+ into 2 groups according to their LID: no effective LID group (eCT+ I+) and effective LID group (eCT+ I-) (strict low iodine diet for more than 2 weeks).

The I/Cr data collected in this study were all measurement data expressed by median (interquartile range IQR), and the data did not conform to normal distribution after the Kolmogorov–Smirnov normality test. Therefore, the Mann-Whitney U rank test was used to analyze the difference of I/Cr between the two groups. Kruskal-Wallis H rank sum test was used to analyze the difference of I/Cr among three or more groups. Analysis of variance was used to compare the differences in age among the groups. The difference was considered statistically significant when $P < 0.05$.

3. RESULTS

1. Patient baseline characteristics: 467 urine samples were collected from 269 patients in this study, including 114 patients collected once, 144 patients collected twice, 19 patients collected three times, and 2 patients collected four times. The interval between each urine sample collection was at least one month. There were 126 urine samples from male patients and 341 urine samples from female patients. The age of patients ranged from 23 to 77 years, with an average of 45 ± 12 years. There were 163 samples in the eCT- group and 304 samples in the eCT+ group, and there was no significant difference in age among the subgroups ($F = 0.48$, $P = 0.694$) and ($F = 0.67$, $P = 0.650$) (Table 1).

2. The comparison of urinary iodine levels between enhanced CT and non-enhanced CT patients and the results of the Kruskal-Wallis H rank sum test for comparative I/Cr levels of eCT+ and eCT-patients are shown in Tables 2 and 3, respectively.

3. The changes in urinary iodine before and after LID in the eCT- group are shown in Fig. (2). I/Cr was 106.86(IQR:59.40) $\mu\text{g/gCr}$ ($n=53$) in I+ group; I/Cr was 42.50(IQR:42.96) $\mu\text{g/gCr}$ ($n=18$) in I- 2W group; I/Cr was 34.96(IQR:38.95) $\mu\text{g/gCr}$ ($n=47$) in I- 4W group; I/Cr was 27.07(IQR:30.22) $\mu\text{g/gCr}$ ($n=45$) in I- ≥ 6 W group. There were significant differences between I+ group and others ($P<0.05$): I+ VS I- 2W $\chi^2= 4.60$, $P=0.0001$; I+ VS I- 4W $\chi^2=7.07$, $P=0.0001$; I+ VS I- ≥ 6 W $\chi^2=7.99$, $P=0.0001$. There was no significant difference among I- groups (I- 2W, I- 4W, I- ≥ 6 W) ($P>0.05$): I- 2W VS I- 4W $\chi^2=0.59$, $P=0.557$; I- 2W VS I- ≥ 6 W $\chi^2=1.31$, $P=0.190$; I- 4W VS I- ≥ 6 W $\chi^2=0.97$, $P=0.331$. Since there was no significant difference among the I- subgroups, all the LID patients were merged into the non-enhanced CT and effective LID group (eCT- I-), and I/Cr was 32.60(IQR:33.96) $\mu\text{g/gCr}$ ($n=110$).

4. The changes of urinary iodine in the eCT + group are shown in Fig. (3). I/Cr was 425.06(IQR:135.30) $\mu\text{g/gCr}$ ($n=14$) in 0.5M eCT+ group, I/Cr was 157.34(IQR:117.04) $\mu\text{g/gCr}$ ($n=90$) in 1M eCT+ group. I/Cr was 91.19(IQR:93.25) $\mu\text{g/gCr}$ ($n=46$) in 2M eCT+; I/Cr was 39.79(IQR:55.87) $\mu\text{g/gCr}$ ($n=128$) in 3M eCT+. I/Cr was 37.76 (IQR:34.00) $\mu\text{g/gCr}$ ($n=26$) in ≥ 4 M eCT+. No significant difference was found only between 3M eCT+ and ≥ 4 M eCT+ ($\chi^2= 0.47$, $P=0.638$).

Table 2. Comparison of urinary iodine levels between enhanced CT and non-enhanced CT patients.

Enhanced CT Status	Subgroup	n	I/Cr($\mu\text{g/gCr}$)	p value
eCT-	I+	53	106.86	0.0412
	I- (2W)	18	42.50	0.0351
-	I (4W)	47	34.96	0.0211
-	I (6W)	45	27.07	0.0349
eCT+	0.5 month	14	425.06	0.0258
	1 month	90	157.34	0.105
	2 months	46	91.19	0.004
	3 months	128	39.79	0.036
	≥ 4 months	26	37.76	0.002

Notte: eCT: non-enhanced CT; eCT+: enhanced CT; I: no effective low iodine diet (LID); I-: effective LID; I/Cr: urinary iodine/urinary creatinine ratio.

Table 3. Kruskal-wallis H rank sum test for comparative I/Cr levels of eCT+ and eCT- patients.

Groups	χ^2	H Statistics	df	p
I+ VS I- 2W	4.60	0.0083	2	0.0001
I+ VS I- 4W	7.07	0.0108	2	0.0001
I+ VS I- ≥ 6 W	7.99	0.0096	2	0.0001
I- 2W VS I- 4W	0.59	0.0078	2	0.557
I- 2W VS I- ≥ 6 W	1.31	0.0080	2	0.190
I- 4W VS I- ≥ 6 W	0.97	0.0061	2	0.331
0.5M eCT+ VS eCT- I+	3.22	0.0087	2	0.001
1M eCT+ VS eCT- I+	2.18	0.0094	2	0.029
2M eCT+ VS eCT- I+	0.76	0.0101	2	0.447
3M eCT+ VS eCT- I+	7.03	0.0100	2	0.0001
≥ 4 M eCT+ VS eCT- I+	5.22	0.0095	2	0.0001

5. The comparison of I/Cr levels between eCT+ patients and eCT- patients is shown in Table 1. 0.5M eCT+ group was significantly higher than eCT- I+ group ($\chi^2=3.22$, $P=0.001$); 1M eCT+ group was also significantly higher than eCT- I+ group ($\chi^2=2.18$, $P=0.029$); There was no significant difference between 2M eCT+ group and eCT- I+ group ($\chi^2=0.76$,

$P=0.447$). 3M eCT+ group was significantly lower than that of the eCT- I+ group ($\chi^2=7.03$, $P=0.0001$), and close to that of the eCT- I- group ($\chi^2=1.76$, $P=0.079$); ≥ 4 M eCT+ group was significantly lower than the eCT- I+ group ($\chi^2=5.22$, $P=0.0001$) and close to the eCT- I- group ($\chi^2=0.58$, $P=0.560$).

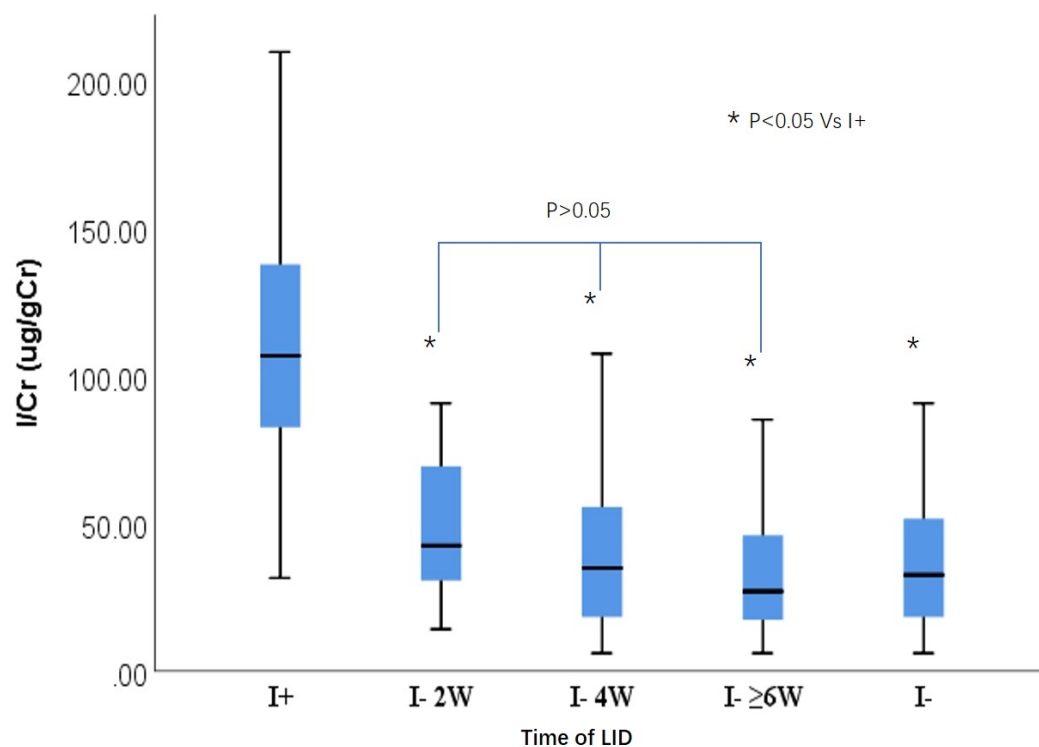


Fig. (2). Change of urinary iodine level for different time of low iodine diet [LID] in patients without enhancement [eCT-]. I+: No LID group; I- 2W: 2 weeks of LID group; I- 4W: 4 weeks of LID group; I- ≥ 6 W: ≥ 6 weeks of LID group. I-: The data were collected from I- 2W, I- 4W and I- ≥ 6 W.

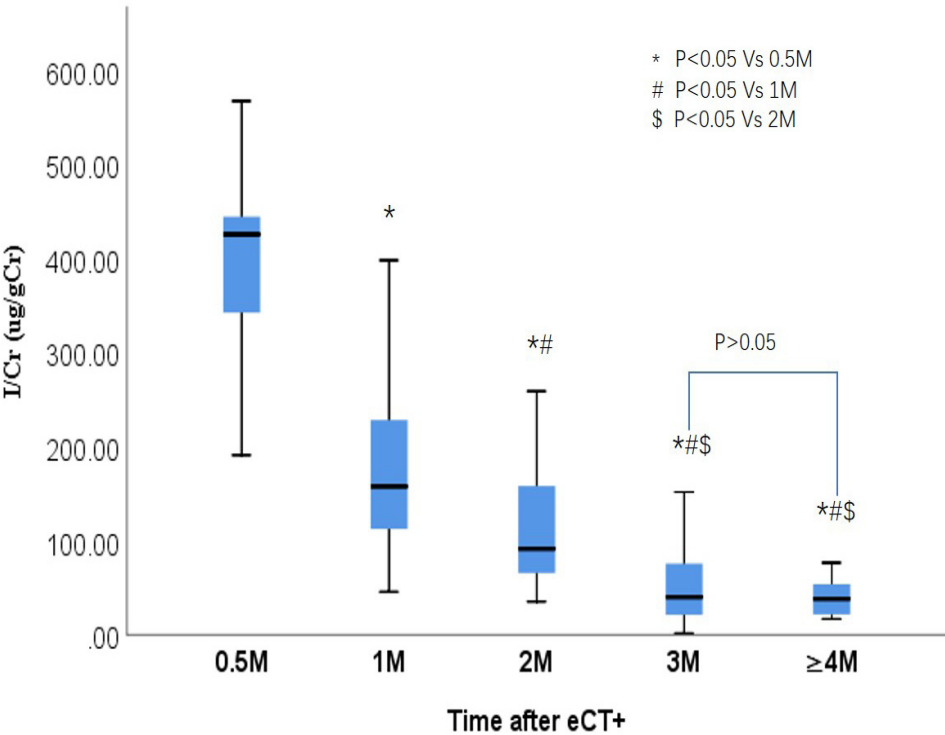


Fig. (3). Changes of urinary iodine level at different time in patients after enhanced CT [eCT+].0.5M: 0.5 month after eCT+; 1M: 1 month after eCT+; 2M: 2 months after the eCT+;3M: 3 months after the eCT+; ≥4M: ≥4 months after eCT+.

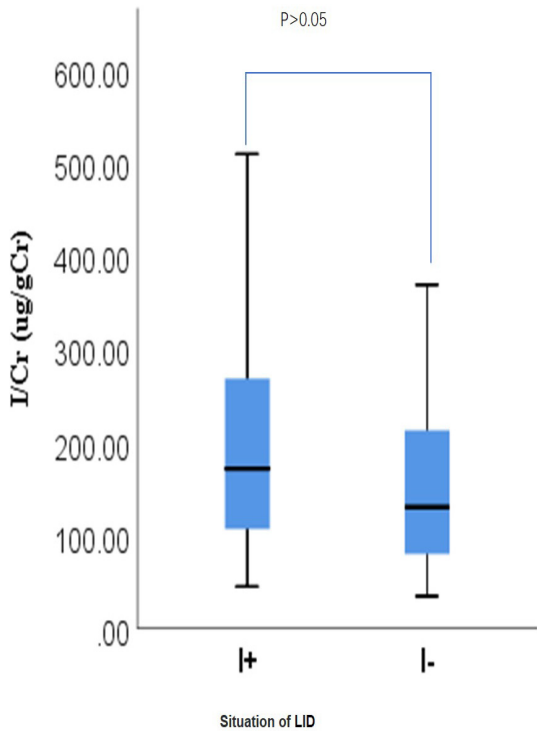


Fig. (4). Comparison of urinary iodine level within 2 months after enhanced CT [eCT +] with or without low iodine diet [LID]. I+: no effective LID; I-: effective LID.

6. The relationship between effective LID and urinary iodine within 2 months after eCT+ is shown in Fig. (4). I/Cr was 172.02[IQR:163.55] $\mu\text{g/gCr}$ [n=70] in the I+ group; I/Cr

was 130.74 [IQR:134.09] $\mu\text{g/gCr}$ [n=80] in the I- group. There was no significant difference between the two groups [$\chi^2=1.79$, P=0.073].

7. Non-enhanced CT patients showed a statistically significant decrease in urinary iodine levels over time (Fig. 5), while enhanced CT patients also showed a decrease in urinary

iodine levels over time (Fig. 6), but this difference was not statistically significant. A negative correlation is observed between urine iodine levels and time, as depicted in Fig. (7).

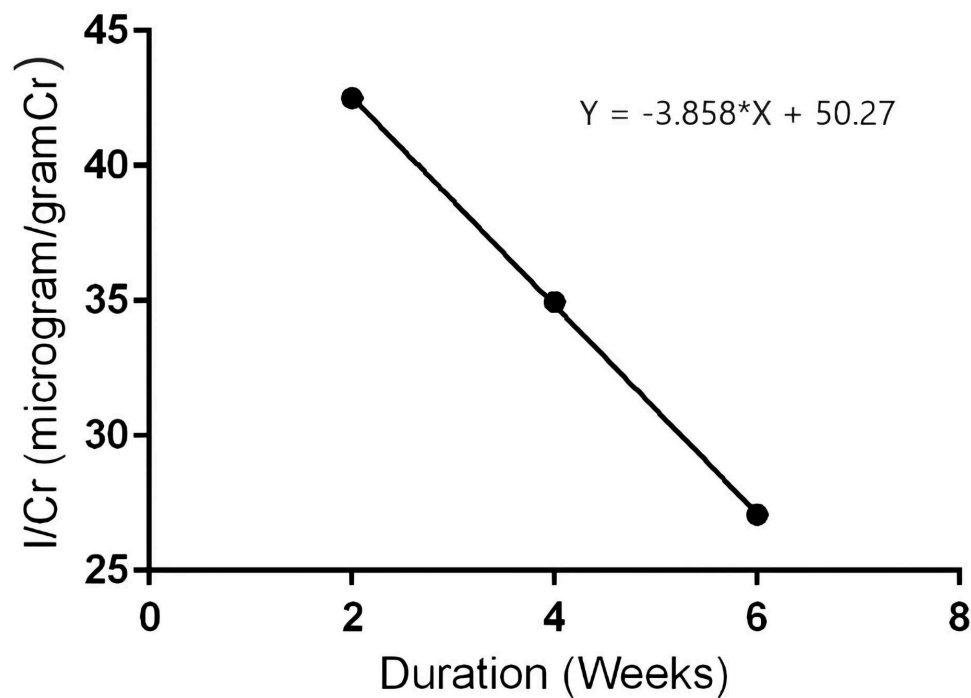


Fig. (5). Scatter plot for urinary Iodine Levels in non-enhanced CT subgroups.

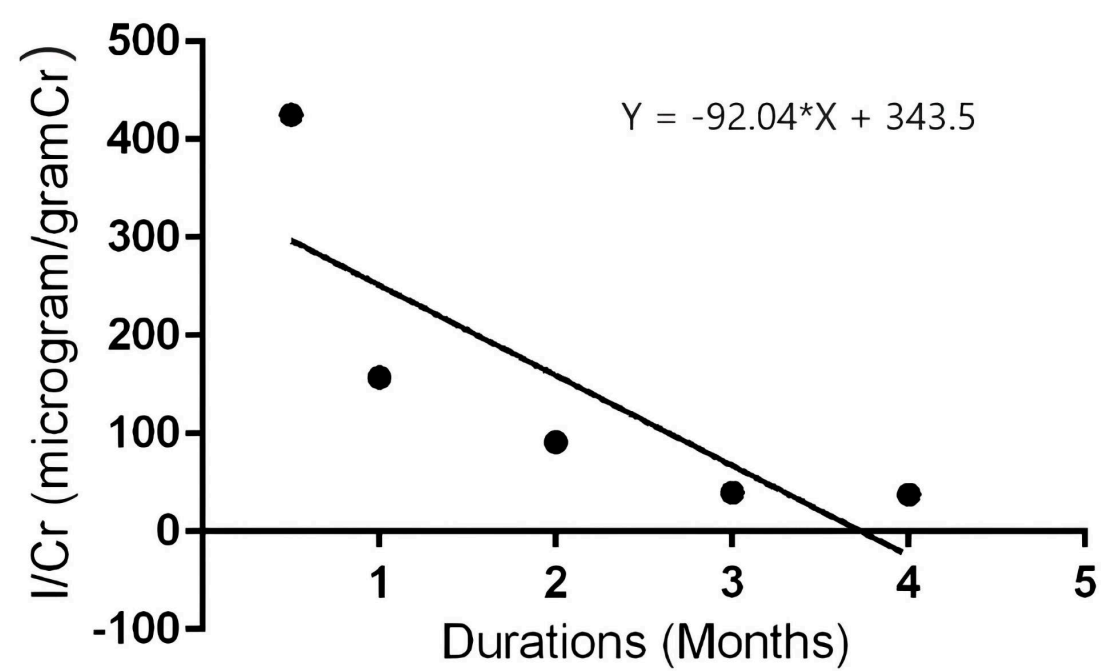


Fig. (6). Scatter plot for urinary Iodine Levels in enhanced CT subgroups.

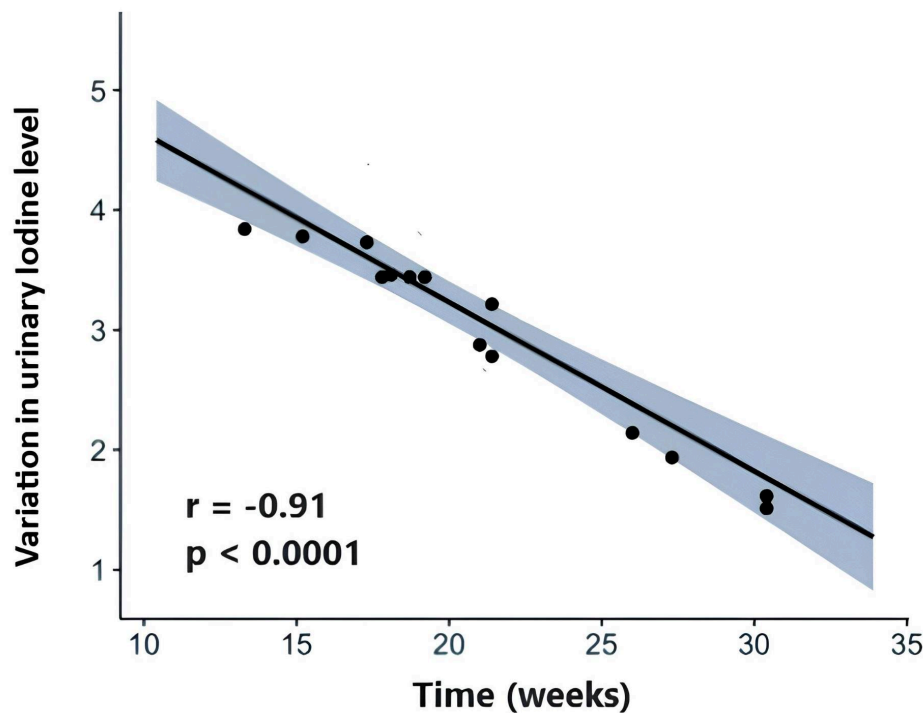


Fig. (7). Correlation scatter plot for variation in urinary iodine level with time.

4. DISCUSSION

The pre-treatment iodine level in the body is a significant determinant of the effectiveness of Radioactive Iodine Therapy (RAIT) [11]. According to a report in 1975, it was observed that LID has the potential to enhance ^{131}I iodine absorption by a range of 17% to 233%, extend the effective half-life of ^{131}I iodine, and elevate the absorbed dosage by a range of 51% to 146% [12]. In a study conducted by Pluijmen *et al.*, a total of 120 patients with differentiated thyroid cancer (DTC) and no evidence of distant metastases were examined. The researchers observed that the 24-hour urine iodine levels were $26.6\mu\text{g}$ in the low-iodine diet (LID) group, whereas the control group exhibited levels of $158.8\mu\text{g}$. According to the study, the LID group had a success rate of 65% in effectively eliminating remaining thyroid tissue by RAIT, whereas the control group only achieved the intended outcome in 48% of cases [13]. The study conducted by Kim *et al.* demonstrated that an iodine-to-creatinine (I/Cr) threshold of more than $66.2\mu\text{g}/\text{G Cr}$ indicated poor preparation of an iodine-free meal. The sensitivity of this threshold was found to be 96.4%, with a specificity of 83.6%. Additionally, the positive predictive value was determined to be 50.0%, while the negative predictive value was calculated to be 99.3% [14]. In the present investigation, it was observed that the average I/Cr value exceeded $66.2\mu\text{g}/\text{gCr}$ among individuals who did not have contrast-enhanced CT scans, and the use of iodine was not restricted. In patients who had contrast-enhanced CT, the concentration of I/Cr was found to exceed $66.2\mu\text{g}/\text{gCr}$ during a period of two months. Nevertheless, the limited sample size of RAIT patients exhibiting I/Cr levels exceeding $66.2\mu\text{g}/\text{gCr}$, along with the absence of comprehensive follow-up data, renders it unfeasible to assess the potential influence on the efficacy of RAIT

treatment. Consequently, further investigation will be conducted after a larger patient cohort and more extensive follow-up data have been accumulated.

In relation to the preparation of a low-iodine diet (LID) prior to radioactive iodine therapy (RAIT), some studies have indicated that the iodine storage level in the majority of patients may be sufficiently decreased to meet the treatment criteria of RAIT during a period of 1-2 weeks of adhering to LID [15]. Additionally, the present study observed a decrease in urine iodine levels among individuals who did not have enhanced CT scans during a two-week period of low iodine diet (LID). Furthermore, it was determined that the urinary iodine levels did not exhibit additional reduction with maintained adherence to the LID. This implies that patients with differentiated thyroid cancer (DTC) who do not have enhanced computed tomography (CT) scans and are scheduled to undergo radioactive iodine therapy (RAIT) following surgery may be eligible for RAIT after strictly adhering to a low-iodine diet (LID) for a period of two weeks.

According to some national recommendations on the diagnostic and treatment criteria for thyroid cancer, it is recommended that thyroid lesions be routinely evaluated using enhanced CT scanning, provided there are no contraindications for the use of iodinated contrast media [3, 4, 9]. Nevertheless, the iodine concentration in iodinated contrast medium ranges from 150 to 370 mg/mL. Even with a relatively low dosage of 30 mL at a concentration of 300 mg/mL, the administration of iodine can result in a total consumption of 9000 milligrams. The administration of iodinated contrast media to patients can lead to a substantial elevation in blood iodine levels and tissue iodine content. Additionally, the presence of iodine within

iodinated contrast media might cause a delay in the subsequent radioactive iodine therapy (RAIT). Currently, there is a lack of unanimous agreement on the duration for which the body's iodine level can be decreased to meet the requirements of RAIT (Radioactive Iodine Therapy) in patients who have undergone enhanced CT scans. Some researchers argue that a period of 4-6 weeks following enhanced CT is sufficient [16, 17]. In a study involving 82 patients diagnosed with lung metastases from differentiated thyroid cancer (DTC), the patients were categorized into three groups based on whether they underwent an enhanced computed tomography (CT) scan prior to receiving radioactive iodine therapy (RAIT), as well as the time interval between the scan and treatment. These groups included the interval < 3 months group, the interval ≥ 3 months group, and the group that did not undergo an enhanced CT scan. The findings indicated a notable disparity in the positive rate of ^{131}I scanning between patients with an interval of less than 3 months and the other two groups (62.5%, 88.9%, and 87.0%). This discrepancy serves as evidence that the administration of iodine-containing contrast medium within 3 months prior to RAIT has an impact on the uptake of ^{131}I by lung lesions in patients [18].

At present, there are few reports about the effect of iodine-containing contrast agents on RAI treatment in DTC patients. The use of iodized contrast agents before RAI treatment will have an impact on RAI uptake in DTC patients. However, large sample data and long-term observation and follow-up data are still needed to confirm the effect of RAI uptake in DTC patients. Research has progressed on low iodine preparation for radioactive iodine therapy in differentiated thyroid carcinoma. . Therefore, without delaying the treatment time, we should try to keep the iodine in the body stable at a low level to ensure the efficacy of RAI.

In light of the ongoing controversy, we conducted a comprehensive investigation to assess the iodine levels of patients at various intervals following enhanced CT scans. Our objective was to elucidate the effects of enhanced CT on the iodine levels of patients with differentiated thyroid cancer (DTC) after surgery. Additionally, we aimed to establish a reliable reference point for determining the optimal timing of radioactive iodine therapy (RAIT) for DTC patients who underwent enhanced CT examinations post-surgery.

The assessment of iodine storage in the body often relies on the measurement of the 24-hour total urinary iodine level. However, the collection of all urine produced by patients over a 24-hour period, which is necessary for monitoring urinary iodine levels, can be challenging to carry out. Prior research has indicated that the utilization of random urine samples for assessing I/Cr can effectively account for variations in water content and urine dilution across people. This method can serve as a substitute for the 24-hour urinary iodine level in evaluating the body's iodine storage levels [14]. Hence, the present study employed the usage of I/Cr as a metric for quantifying the concentration of iodine contained inside the human body.

The present study revealed a gradual decrease in urinary iodine levels following enhanced CT. However, even after one month, the urinary iodine levels remained significantly elevated compared to the general population without a low

iodine diet (LID). It was observed that urinary iodine levels could be reduced to the level observed in non-enhanced CT patients following a general diet after two months of enhanced CT. The primary route of iodine excretion in the human body is renal excretion. Prior research has indicated that people with normal renal function have a peak in urine iodine concentration around 1.1 ± 0.5 weeks after the administration of iodine-containing contrast media. Subsequently, it takes approximately (5.2 ± 4.0) weeks for the urinary iodine concentration to recover to its normal baseline level [19]. The *in vivo* iodine excretion rate aligns with the pharmacokinetic properties of an initial rapid phase followed by a subsequent slower phase. The rate of excretion has a tendency to reach a state of stability about 30 days following administration, with the subsequent elimination half-life estimated to be approximately 45 days [20]. Hence, the excretion rate of iodine exhibited a decrease over the two-month period following contrast-enhanced CT, in comparison to the excretion rate seen in the absence of contrast-enhanced CT. The findings of this study indicate that the urinary iodine levels in patients who underwent contrast-enhanced CT for a duration of 3 months and followed a low-iodine diet (LID) for more than 2 weeks were similar to those observed in patients who did not undergo contrast-enhanced CT. Similarly, the urinary iodine levels in patients who underwent contrast-enhanced CT for a duration of 4 months and followed a LID for more than 2 weeks were comparable to those observed in patients without contrast-enhanced computed tomography. The findings of our study indicate that the levels of iodine reserves following contrast-enhanced CT scans stay elevated, decrease gradually, and need a waiting period of three months to achieve levels equivalent to those observed in individuals who did not have contrast-enhanced CT scans. This study further discovered that despite the successful prohibition of iodine or low-iodine diet (LID) throughout a two-month period following enhanced CT, the body's iodine storage remained greater compared to individuals who did not receive enhanced CT and did not adhere to LID. Therefore, there was no separate study for each group within a two-month period following enhanced CT. Prior research has indicated that the use of radioiodine ablation therapy (RAIT) three months post-surgery did not impact the therapeutic outcome for patients with varying levels of recurrence risk following differentiated thyroid cancer (DTC) surgery [21, 22]. Hence, it is important to maintain stable iodine levels in patients' bodies for a minimum of two months subsequent to enhanced CT in order to optimize the effectiveness of Radioactive Iodine Therapy (RAIT). Consequently, it is advised to refrain from expediting the follow-up of the RAIT process. The findings of this study indicate that individuals who plan to undergo radioactive iodine therapy (RAIT) following the diagnosis of differentiated thyroid cancer (DTC) should receive treatment around three months after undergoing an improved computed tomography (CT) scan.

CONCLUSION

The results of this study show that DTC patients who underwent eCT scan and intended to undergo RAIT needed to wait for more than three months and a strict low iodine diet for more than two weeks to reduce the level of iodine *in vivo* to

ensure therapeutic effect.

AUTHORS' CONTRIBUTIONS

SF: Concept and designed the study, SH: Data Collection, PZ: Data Analysis, CZ: Writing article, Proofreading, and final editing along with guarantor of the manuscript.

LIST OF ABBREVIATIONS

DTC	=	Differentiated Thyroid Cancer
eCT	=	Enhanced Computed Tomography
CT	=	Computed Tomography
LID	=	Low Iodine Diet

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee of the Zhejiang University School of Medicine (protocol ZU # RC/IRB/2022/1064).

HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants of this study.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

No animals were used that are the basis of this study. Upon a reasonable request, the corresponding author (C.Z) will provide access to the requested information.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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