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Effects of high-activity radioactive iodine treatment on renal function in patients with differentiated thyroid carcinoma — retrospective study

Liang Yin[1, 2]*, Weilong Li[1, 3]*, Xiaolan Lv[1, 4]*, Yangyang Lin[5]*, Qiang Jia[1], Jian Tan[1], Xue Li[1], Danyang Sun[1], Yan Wang[6], Zhaowei Meng[1]

[1]*Department of Nuclear Medicine, Tianjin Medical University General Hospital, Tianjin, China*
[2]*Department of Nuclear Medicine, Pingjin Hospital, Characteristic Medical Centre of Chinese People's Armed Police Forces, Tianjin, China*
[3]*Department of Nuclear Medicine, The Affiliated Yantai Yuhuangding Hospital of Qingdao University, Yantai, China*
[4]*Department of Ultrasound, Affiliated Hospital of Hebei University, Baoding, China*
[5]*Department of Dermatology, Tianjin Children' s Hospital, Tianjin, China*
[6]*State Key Laboratory of Component-based Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin, China*
**These co-first authors contributed equally to the paper.*

Abstract

Introduction: It is not clear whether high-activity radioactive iodine (^{131}I) treatment will affect renal function. This study aimed to investigate the effects of high-activity ^{131}I treatment on the clinical metrics of renal function in patients with differentiated thyroid carcinoma (DTC).
Material and methods: 262 DTC patients with abnormal baseline renal function (group A) and 262 DTC patients with normal baseline renal function (group B) who received ^{131}I therapy were analysed. Each group was further divided into three subgroups based on the cumulative activity of ^{131}I: subgroup 1 if the cumulative activity was less than 11.1 GBq; subgroup 2 if the cumulative activity was between 11.1 GBq and 18.5 GBq; and subgroup 3 if the cumulative activity was more than 18.5 GBq. The clinical metrics of renal function including serum creatinine (SCr), blood urea nitrogen (BUN) and estimated glomerular filtration rate (eGFR) were measured and compared before initial ^{131}I treatment and 5 years later.
Result: There was no significant difference of the demographics between the two groups. In group A, SCr and BUN levels were elevated in 186 and 113 patients, respectively, and eGFR was decreased in 108 patients before the initial ^{131}I therapy. SCr and BUN levels were found to be increased in all subgroups 5 years after the initial ^{131}I therapy; furthermore, eGFR was found to be decreased in all subgroups after ^{131}I therapy, and the difference was statistically significant ($p < 0.05$). A gender bias was not observed in the changing trends of SCr and BUN levels and eGFR. In group B, no significant difference in the mean levels of SCr, BUN, and eGFR was observed in the 3 subgroups ($p > 0.05$), regardless of gender, before the initial ^{131}I therapy and 5 years later. A total of 5, 2, and 2 patients presented with abnormal renal function after ^{131}I treatment in subgroups 1, 2, and 3, respectively. No statistically significant difference was observed in the incidence of renal dysfunction among the 3 subgroups ($p = 0.423$).
Conclusion: Our findings suggest that the nephrotoxicity of high-activity ^{131}I therapy, regardless of gender, is very low in patients with DTC with normal renal function; however, high-activity ^{131}I therapy may exacerbate the loss of renal function in those with renal dysfunction. **(Endokrynol Pol 2022; 73 (3): 619–626)**

Key words: *blood urea nitrogen; creatinine; differentiated thyroid carcinoma; estimated glomerular filtrate; radioactive iodine*

Introduction

The incidence of thyroid cancer is increasing worldwide, and the most common histological subtype of thyroid cancer is papillary carcinoma followed by follicular carcinoma. The carcinomas are collectively referred to as well-differentiated thyroid carcinoma (DTC). The definitive therapy for DTC includes surgical thyroidectomy, with or without adjuvant ^{131}I therapy depending on histological information and the presence of residual, unresectable, and metastatic disease [1–3]. ^{131}I therapy has been successfully applied for more than 60 years for the management of DTC. Various studies have proven that ablative ^{131}I therapy significantly reduces the frequency of recurrences and tumour spread in patients with thyroid cancer. In patients with distant metastases, approximately 50% complete response may be achieved with ^{131}I treatment [4].

The well-known possible side effects of high-activity ^{131}I therapy include radiation thyroiditis, nausea, vom-

Zhaowei Meng, MD, PhD, Department of Nuclear Medicine, Tianjin Medical University General Hospital, Anshan Road No. 154, Heping District, Tianjin, China, 300052; Tel: 86-18622035159, fax: 86-022-27813550; e-mail: zmeng@tmu.edu.cn or jamesmencius@163.com; e-mail: jamesmencius@163.com
Yan Wang, PhD, State Key Laboratory of Component-based Chinese Medicine, Tianjin University of Traditional Chinese Medicine, China; e-mail: wangyan@tjutcm.edu.cn

iting, sialadenitis, xerostomia, dental caries, long-term dysphagia, nasolacrimal duct obstruction, increased risk of leukaemia, secondary cancers, and pulmonary fibrosis in advanced stages [3, 5, 6]. Considering that ^{131}I is eliminated from the body mainly by the kidneys, the pathway potentially exposes the associated organs to radiation [7]. Moreover, the sodium/iodide symporter (NIS) protein that accumulates ^{131}I has been found in the kidneys, primarily in the distal tubular system; it is present at a low concentration in the proximal tubules and is absent in the glomeruli [8]. However, most patients with DTC exhibit a long life expectancy; hence, the use of ^{131}I therapy has raised concern regarding its potential for developing renal dysfunction. It is critical to comprehensively define the risk of renal impairment caused by ^{131}I in such patients. To our knowledge, the current literature lacks published data regarding the nephrotoxicity of radioiodine owing to high-activity ^{131}I treatment. However, with regard to the quality of life, it is important to explore whether relevant nephrotoxicity is caused by ^{131}I therapy. The aim of this study is to examine whether high-activity ^{131}I used for the treatment of DTC can result in any change in the metrics of renal function during a relatively long period.

Material and methods

Patients

262 DTC patients complicated with abnormal baseline renal function admitted for the high-activity ^{131}I treatment at the Department of Nuclear Medicine, Tianjin Medical University General Hospital from January 2007 to December 2016 were enrolled as group A. Based on the principle of age, sex, body mass index (BMI), and cumulative activity matching, 262 DTC patients with normal baseline renal function admitted for the high-activity ^{131}I treatment were enrolled as group B.

The metrics of renal function, including blood urea nitrogen (BUN; normal range, 3.1–8.0 mmol/L) and serum creatinine (SCr; normal range, 57–97 μmol/L) levels and estimated glomerular filtration rate (eGFR), were evaluated using the Modification of Diet in Renal Disease (MDRD) equation [9]. Based on the metrics of renal function, abnormal renal function was defined as patients with SCr levels > 97 μmol/L and/or BUN levels > 8.0 mmol/L (based on the reference standard of the clinical laboratory of Tianjin Medical University General Hospital) and/or eGFR < 60 mL/min/1.73 m^2 (based on the chronic kidney disease criteria) [10]. Normal renal function was defined as patients with SCr levels ≤ 97 μmol/L, BUN levels ≤ 8.0 mmol/L, and eGFR ≥ 60 mL/min/1.73 m^2.

^{131}I therapy, follow-up, and grouping

All patients had undergone total or near-total thyroidectomy and received ^{131}I treatment for the first time. ^{131}I was administered at an activity of 2.59–7.40 GBq at each time to all patients after thyroid hormone withdrawal (THW) 3–4 weeks. After the administration of ^{131}I, the patients were asked to drink more water and urinate more frequently. If required, subsequent ^{131}I activities were administered every 6–12 months. None of the patients received external irradiation to the abdomen in both the groups.

The ^{131}I treatment of all patients ended within 4 years, and all patients were followed up for 5 years after the initial treatment. The follow-up (FU) was continued based on clinical examination; neck ultrasonography; hepatorenal function; and blood tests for thyroid hormones including thyroid-stimulating hormone (TSH) and thyroglobulin (Tg), anti-Tg, and anti-thyroperoxidase antibodies. All renal function parameters were evaluated using an automated analyser (Siemens Viva-ProE). SCr and BUN levels and eGFR evaluated 3–4 weeks after THW for the initial ^{131}I treatment were used as baseline values. Five years later, the post-therapy SCr and BUN levels and eGFR evaluated 3–4 weeks after THW for diagnostic ^{131}I scanning were used as the "5-year FU" values. The data were systematically recorded in clinical records, and they were collected at least once per year.

Based on different cumulative activity of ^{131}I, the two groups were further divided into three subgroups, namely: subgroup 1 if the cumulative activity was less than 11.1 GBq; subgroup 2 if the cumulative activity was between 11.1 GBq and 18.5 GBq; and subgroup 3 if the cumulative activity was more than 18.5 GBq. The study was approved by Ethics Committee of Tianjin Medical University General Hospital, and patients provided written informed consent to participate in the study.

Statistical analysis

The statistical analysis was performed on SPSS 22.0. The distribution of all parameters was found to be normal. The results were reported as mean ± standard deviation (SD). The changes in parameters among the 3 subgroups were evaluated using repeated measures analysis of variance (ANOVA). The comparison between baseline and follow-up levels of SCr and BUN and eGFR or the comparison of values among the groups or subgroups was analysed using Student's t-test. Fisher's exact test was used for comparing the incidence of renal insufficiency among the subgroups after ^{131}I therapy. Two-tailed p values < 0.05 were considered to indicate statistically significant relationships.

Results

The demographic including age, histological subtype, purpose of treatment, BMI, sex, cumulative activity of ^{131}I and number of treatments of group A and B patients were reported in Table 1. No significant difference between the 2 groups was found for any of the 7 parameters.

In group A, SCr and BUN levels were elevated in 186 and 113 patients, respectively, and eGFR < 60 mL/min/1.73 m^2 was found in 108 patients. Before the initial ^{131}I therapy, there was no significant difference in the 3 renal function parameters, the age, BMI, and sex among the 3 subgroups. SCr and BUN levels were found to be increased in all subgroups 5 years after the initial ^{131}I therapy compared with the levels before treatment. The higher the cumulative activity, the greater the observed increase in SCr and BUN levels; the difference was statistically significant. Furthermore, eGFR was found to be decreased in all groups after ^{131}I treatment, and the greater the cumulative activity, the greater the observed decrease in eGFR; the difference was statistically significant. However, a gender bias was not observed in the changing trends of SCr and BUN levels and eGFR. The results of biochemical parameters are summarised in Tables 2–4.

In group B, no significant difference was observed in the mean levels of SCr and BUN and eGFR in subgroups

Table 1. *The age, histological subtype, purpose of treatment, body mass index (BMI), sex, cumulative activity of ^{131}I, and number of treatments in patients with differentiated thyroid carcinoma of group A and B*

No.	Group A	Group B
	262	262
Histological subtype of thyroid cancer		
Papillary	222	224
Follicular	40	38
Purpose of treatment		
Ablation of the thyroid remnant	189	192
Tumour recurrence and/or metastatic disease	73	70
Age		
Year (mean ± SD)	45.6 ± 12.5	46.1±11.8
Range	17–75	17–73
Sex		
Male	122	122
Female	140	140
BMI		
Mean ± SD	25.9 ± 3.5	25.7 ± 3.8
Range	18.3–39.5	19.0–45.8
Cumulative activity of ^{131}I		
GBq (mean ± SD)	10.19 ± 7.19	10.27 ± 6.99
Range	2.59–44.77	2.59–45.14
Number of treatments		
Mean ± SD	2.69 ± 1.67	2.68 ± 1.56
Range	1–9	1–9

SD — standard deviation

1, 2, and 3, regardless of gender, before the initial ^{131}I therapy or 5 years later. The clinical metrics of renal function are summarised in Table 5. A total of 9 (3.4%) patients developed renal function impairment 5 years later, which was defined as SCr levels > 97 μmol/L, BUN levels > 8.0 mmol/L, or eGFR < 60 mL/min/1.73 m^2; this means that 5, 2, and 2 patients presented with abnormal renal function in subgroups 1, 2, and 3, respectively. No statistically significant difference was observed in the incidence of renal dysfunction among the 3 subgroups (Tab. 6). In subgroup 3, 4 patients received a cumulative activity of more than 37 GBq and none of them presented with abnormal renal function after ^{131}I therapy. The patients who developed renal impairment were older than those who did not (age 60.1 ± 11.6 years versus 45.7 ± 11.5 years, respectively; p = 0.000), and the difference was statistically significant. In all patients, the absolute increase in SCr and BUN levels was 0.87 μmol/L and 0.10 mmol/L, respectively, and the absolute decrease in eGFR was 3.17 mL/min/1.73 m^2.

Discussion

We compared the renal function parameters between ^{131}I pre-therapy and post-therapy patients. It should be emphasized that this is a retrospective study that used a database not specifically designed for this protocol because it is virtually impossible to design a prospective study on the nephrotoxicity of ^{131}I therapy owing to the long timespan involved. In this retrospective study, we investigated 524 patients treated with ^{131}I. In 262 patients with normal renal function, our findings revealed a non-statistically significant change in the mean values of renal function parameters (SCr, BUN, and eGFR) after ^{131}I treatment compared with baseline values, regardless of gender. We did not find an association between radiation exposure and the incidence of renal dysfunction despite the administration of a higher activity of ^{131}I.

Table 2. *Measurement results of serum creatinine (SCr) levels before and 5 years after initial ^{131}I treatment of patients with differentiated thyroid carcinoma with increased SCr levels*

Group A	n	SCr [μmol/L]	
		Baseline	5-year FU
Subgroup 1	134	109.59 ± 16.73	111.75 ± 18.52 (p = 0.002)
Male	66	108.14 ± 9.10	110.18 ± 13.10 (p = 0.016)
Female	68	111.00 ± 21.71	113.26 ± 22.57 (p = 0.037)
Subgroup 2	29	111.58 ± 21.60	122.07 ± 25.51 (p = 0.000)[a]
Male	15	110.47 ± 10.61	121.67 ± 14.71 (p = 0.000)
Female	14	112.79 ± 29.67	122.50 ± 34.18 (p = 0.000)
Subgroup 3	23	112.00 ± 19.90	141.83 ± 29.67 (p = 0.000)[b]
Male	12	112.83 ± 15.09	138.25 ± 22.51 (p = 0.000)
Female	11	111.09 ± 24.89	145.73 ± 36.71 (p = 0.000)

[a]subgroup 2: subgroup 1 (p = 0.019); [b]subgroup 3: subgroup 2 (p = 0.001); FU — follow-up

Table 3. *Measurement results of blood urea nitrogen (BUN) levels before and 5 years after initial ^{131}I treatment of patients with differentiated thyroid carcinoma with increased BUN levels*

Group A	n	BUN [mmol/L]	
		Baseline	5-year FU
Subgroup 1	74	9.53 ± 1.27	9.84 ± 1.74 (p = 0.001)
Male	39	9.74 ± 1.53	10.09 ± 2.09 (p = 0.020)
Female	35	9.28 ± 0.84	9.56 ± 1.21 (p = 0.011)
Subgroup 2	29	9.24 ± 0.91	10.65 ± 1.46 (p = 0.000)[a]
Male	15	9.11 ± 0.70	10.55 ± 1.17 (p = 0.000)
Female	14	9.39 ± 1.10	10.76 ± 1.76 (p = 0.000)
Subgroup 3	10	9.16 ± 1.34	12.21 ± 2.65 (p = 0.000)[b]
Male	6	9.38 ± 1.72	12.47 ± 3.25 (p = 0.006)
Female	4	8.83 ± 0.41	11.83 ± 1.77 (p = 0.026)

[a]subgroup 2: subgroup 1 (p = 0.038); [b]subgroup 3: subgroup 2 (p = 0.018); FU — follow up

Table 4. *Results of estimated glomerular filtration rate (eGFR) before and 5 years after initial ^{131}I treatment of patients with differentiated thyroid carcinoma with decreased eGFR levels*

Group A	n	eGFR (mL/min/1.73 m^2)	
		Baseline	5-year FU
Subgroup 1	75	51.78 ± 7.25	49.08 ± 7.74 (p = 0.000)
Male	13	56.74 ± 2.64	52.51 ± 4.06 (p = 0.000)
Female	62	50.74 ± 7.49	48.36 ± 8.14 (p = 0.000)
Subgroup 2	18	52.18 ± 8.90	44.48 ± 8.68 (p = 0.000)[a]
Male	6	56.70 ± 2.73	48.26 ± 5.76 (p = 0.002)
Female	12	49.92 ± 10.11	42.58 ± 9.47 (p = 0.000)
Subgroup 3	15	50.51 ± 7.65	36.89 ± 11.38 (p = 0.000)[b]
Male	5	54.35 ± 4.35	42.37 ± 4.62 (p = 0.002)
Female	10	48.60 ± 8.39	34.15 ± 6.57 (p = 0.000)

[a]subgroup 2: subgroup 1 (p = 0.027); [b]subgroup 3: subgroup 2 (p = 0.007); FU — follow up

However, high-activity ^{131}I therapy aggravated renal impairment in 262 patients with abnormal renal function. The higher the ^{131}I cumulative activity, the greater the impairment of renal function. A gender bias was not observed in the changing trends of SCr and BUN levels and eGFR.

The kidney is probably the most radiosensitive of the abdominal organs [11]. Although the renal tissue can tolerate some radiation, depending on the dosage and nuclide type, radiation nephropathy owing to renal irradiation has been recognized as an important complication of external beam radiation therapy (EBRT) or internal radiation therapy such as peptide receptor radionuclide therapy (PRRT). Based on the data derived from patients who have undergone EBRT, it is generally accepted that a activity of 23 Gy to the kidneys, in fractions of approximately 2 Gy, leads to a 5% risk of renal failure in patients within 5 years and that an activity of 28 Gy leads to a 50% risk of renal failure within the same period [12]. In addition, other studies have demonstrated that it is difficult to tolerate ionising radiation of more than 25–30 Gy because the outcome can be hazardous [13, 14]. These data cannot be simply translated to internal irradiation therapy with radionuclides. Unlike external radiation, the activity rate in internal isotope therapy is much lower and of a longer duration than that in EBRT. Radionuclides used in vivo generally deliver a radiation activity over an extended period depending on their physical and biological half-lives [15]. Data from various cancer studies, including studies on neuro-endocrine tumours (NETs) and castrate-resistant prostate cancer, provide some insight into renal damage caused by radio pharmaceuticals. In the largest study group about ^{90}Y-labelled peptides, which included 1106 patients, renal toxicity was found to be 9.2% with a maximum follow-up period of 23 months and 8%

Table 5. *Measurement results of renal function metrics of patients in group B before and 5 years after initial radioactive iodine (^{131}I) treatment*

Group B	n	SCr [μmol/L]		BUN [mmol/L]		eGFR [mL/min/1.73 m²]	
		Baseline	5-year FU	Baseline	5-year FU	Baseline	5-year FU
Subgroup 1	188	66.32 ± 13.95	66.95 ± 15.93 (p = 0.468)	3.98 ± 1.15	4.07 ± 1.01 (p = 0.230)	106.49 ± 24.52	103.74 ± 24.03 (p = 0.069)
Male	81	75.47 ± 12.94	76.54 ± 15.93 (p = 0.484)	4.40 ± 1.13	4.53 ± 1.09 (p = 0.347)	108.40 ± 26.70	105.07 ± 25.22 (p = 0.173)
Female	107	59.39 ± 10.23	59.68 ± 11.51 (p = 0.769)	3.66 ± 1.05	3.73 ± 0.78 (p = 0.467)	105.04 ± 22.76	102.73 ± 23.15 (p = 0.229)
Subgroup 2	47	67.38 ± 11.83	68.83 ± 14.06 (p = 0.419)	4.20 ± 1.23	4.23 ± 1.31 (p = 0.854)	106.46 ± 20.80	102.01 ± 19.30 (p = 0.127)
Male	26	73.92 ± 9.87	76.96 ± 13.41 (p = 0.283)	4.63 ± 1.12	4.85 ± 1.19 (p = 0.405)	108.55 ± 22.26	102.64 ± 23.66 (p = 0.161)
Female	21	59.29 ± 8.59	58.76 ± 6.16 (p = 0.794)	3.67 ± 1.17	3.47 ± 1.04 (p = 0.248)	103.88 ± 19.04	101.22 ± 12.48 (p = 0.514)
Subgroup 3	27	66.89 ± 12.11	68.48 ± 13.28 (p = 0.554)	4.09 ± 1.07	4.27 ± 1.29 (p = 0.313)	107.32 ± 20.44	103.41 ± 23.48 (p = 0.393)
Male	15	72.80 ± 10.75	72.47 ± 12.10 (p = 0.913)	4.51 ± 1.11	4.71 ± 1.54 (p = 0.479)	111.15 ± 21.67	109.79 ± 21.83 (p = 0.802)
Female	12	59.50 ± 9.61	63.50 ± 13.49 (p = 0.414)	3.57 ± 0.78	3.73 ± 0.59 (p = 0.465)	102.53 ± 18.57	95.43 ± 23.90 (p = 0.384)

SCr — creatinine; BUN — blood urea nitrogen; eGFR — estimated glomerular filtration rate

Table 6. *Abnormal renal function 5 years after initial radioactive iodine (^{131}I) treatment in three subgroups of patients in group B*

Group B	n	Renal function after 5-year FU		χ^2	p
		Normal	Abnormal		
Subgroup 1	188	183 (181.5)	5 (6.5)	1.721	0.423
Subgroup 2	47	45 (45.4)	2 (1.6)		
Subgroup 3	27	25 (26.1)	2 (0.9)		

FU — follow-up

with a longer follow-up for approximately 157 months, based on plasma creatinine levels and eGFR evaluated with the MDRD formula [16, 17]. In the largest study group of 504 patients about ^{177}Lu-labelled peptides, with a median follow-up of 19 months, serious nephrotoxicity was found to be 0.4% [18]. Anna Yordanova et al. [19] suggest that no relevant increase in nephrotoxicity was detected in patients who received kidney radiation activity > 19 Gy in the follow-up period of the study that used ^{177}Lu-PSMA (prostate-specific membrane antigen) therapy for patients with castrate-resistant prostate cancer. The results of a study demonstrated that very low activity of ^{137}Cs with activities of 4000 or 8000 Bq/kg of internal IR (ionizing radiation) not only induced early renal histological injury and acute oxidative stress but also caused DNA damage [20]. As evident from such studies, each radiopharmaceutical exhibits different potential toxicity and side effects owing to its special biodistribution patterns, dosage, nuclide type, and radiation energy. Adequately water-soluble ^{131}I-labelled radiopharmaceuticals are preferentially excreted through the renal route, with a high renal uptake [21]. Approximately 90% of ^{131}I is excreted in the urine within 48 h of administration [22]. In the ^{131}I experimental trials, Nihat Yumusak et al. [23] demonstrated that cell proliferation and apoptosis began on the seventh day and peaked during the tenth week based on immunohistochemical analyses of the kidneys. Kolbert et al. [24] provided dose-volume histograms and mean absorbed doses for 14 normal organs; the calculations were performed using a 3D voxel-based method. In this study, the mean ^{131}I activity was approximately 0.10 Gy/GBq in the kidneys. In our study, the patients were usually advised to drink plenty of water to reduce the risk of nephrotoxicity after ^{131}I therapy. No obvious renal toxicity was observed in patients with normal renal function. A possible explanation is the limited follow-up time in relation to the longer latency period

from the time of initial treatment to the development of renal dysfunction. The mean age of 9 patients with renal dysfunction was greater than that of patients with normal renal function, which in turn raises speculation regarding radiation damage being more severe in older patients, as is commonly believed [25]. However, significant radiation activity to the kidneys was observed in patients with pre-therapy for renal insufficiency, despite renoprotection. In patients with abnormal renal function before ^{131}I therapy, renal function declined after 5 years, mainly because of poor baseline renal function. However, the higher the cumulative activity, the more severe the renal damage, which indicates that high-activity ^{131}I treatment also leads to the aggravation of renal damage. The excretion of ^{131}I by the kidneys may be reduced in patients with renal insufficiency [26], which may aggravate further damage of renal function. Vogel et al. [27] stipulated that the biological half-life of ^{131}I was significantly influenced by eGFR, and a decrease in GFR may significantly prolong the half-life of ^{131}I. Similarly, in some studies, the prescribed activity of ^{131}I in patients with renal insufficiency is reduced by approximately 30% or 50% to compensate for the prolonged clearance of radioiodine [28–30].

As a traditional method, THW induces transient hypothyroidism and stimulates endogenous TSH secretion. A hypothyroid state causes metabolic effects on every organ system. Decreased haemodynamics in the circulatory system reduced renal blood flow, renal plasma flow, especially GFR. Recent studies have reported similar changes in renal function during THW preparation for ^{131}I treatment [31]. Coura-Filho et al. [32] found an 18–22% decrease in GFR in 14 patients prepared by THW. In our study, baseline renal function and "5-year FU" renal function were measured 3–4 weeks after THW, avoiding the influence of different thyroid function status on renal function.

SCr, an amino acid with a molecular mass of 113 D, which is freely filtered by the glomerulus, is the most commonly used metabolite for the assessment of renal function, despite several drawbacks. SCr levels are affected by several factors, such as body weight, exercise, diet, tumour burden, sex, and muscle mass, which need to be corrected for the accuracy of assessing renal function [33]. The diagnostic sensitivity of SCr evaluation is considered insufficient for analysing moderate GFR reduction. Therefore, the use of SCr levels as a means to assess the renal function levels alone is not recommended. In some studies, post-therapy SCr levels did not increase proportionately with cumulative radioactivity and renal absorbed doses of the kidneys [34]. To date, GFR has been proposed as the standard that should be used for evaluating radiation-induced renal damage [35]. However, the measured GFR was not a feasible marker in the present study because its measurement requires continuous intravenous infusion of an ideal filtration marker such as inulin and multiple blood or urine collections, which is not practical for clinical routine use [36]. Radiopharmaceuticals for renal function measurements such as ^{51}Cr-ethylenediaminetetraacetic acid (EDTA) and ^{99m}Tc-diethylenetriaminepentaacetic acid (DTPA) are expensive, complicated, and time consuming for the follow-up of large patient groups. Owing to the convenience of SCr evaluation, various equations based on SCr have been introduced for the evaluation of eGFR levels in order to overcome such limitations. Three formulae are usually recommended, namely: the MDRD, Cockcroft–Gault (CG), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. MDRD seems to be more reliable [37]; hence, we used it to estimate GFR. However, the accuracy of evaluating eGFR using SCr levels remained questionable. During the initial decrease in GFR, the tubular secretion of creatinine enhances, which can alleviate the increase in SCr levels. Until the tubular secretory capacity is saturated, SCr levels may remain normal and eGFR may be overestimated [38, 39].

Study limitations

The major limitation of this quality study was the unavailability of control data of patients with thyroid cancer who did not receive ^{131}I treatment. Another limitation was the identification of renal dysfunction based on SCr and BUN levels and eGFR instead of measured GFR. Furthermore, GFR gradually decreased with age, and age stratification was not performed in this study. In addition, the evidence derived from a retrospective cohort study is typically lower in statistical quality because of various sources of inherent bias such as surveillance bias, which may result in a classification bias.

Conclusions

In the present study, we found that nephrotoxicity was low in patients with DTC with normal renal function treated with ^{131}I. Although the cumulative activity was approximately 37 GBq, ^{131}I did not cause significant nephrotoxicity in the patients. After we subdivided the patients into 3 subgroups based on the cumulative activity, we failed to demonstrate a statistical difference, and the incidence of renal dysfunction did not achieve a statistically significant level, which was not associated with the cumulative activity. However, our findings revealed an increasing trend in BUN and SCr levels and a decreasing trend in eGFR in patients with renal dysfunction who received ^{131}I treatment. Moreover, the damage to renal function becomes more severe

with an increase in cumulative activity. The present study indicates that close attention should be paid to patients with abnormal renal function before treatment in order to maintain an appropriate balance between therapeutic efficacy and the reduction of nephrotoxicity.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Availability of data and material

The datasets for the present study were from the Department of Nuclear Medicine, Tianjin Medical University General Hospital.

Code availability

Not applicable.

Authors' contributions

L.Y. wrote the manuscript. Co-first authors L.Y., W.L., X.L., and Y.L. contributed equally to the study. Y.W. provide statistical consultation as a statistician. Q.J., J.T., X.L., D.S., and Z.M. revised the manuscript. All authors contributed to manuscript revision, read, approved the submitted version, and agreed to be accountable for all aspects of the research in ensuring the accuracy of this study. All authors have given consent to the publication of this manuscript.

Ethics approval

The research reported in this study that involved human participants was in accordance with the ethical standards of the institution and with the principles of the Declaration of Helsinki 1964 and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from the patients for the anonymous use of their clinical, imaging, and histological data.

Consent for publication

Not applicable.

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