

# Preparation for radioactive iodine therapy is not a risk factor for the development of hyponatremia in thyroid cancer patients

Jahae Kim, MD<sup>a</sup>, Sang-Geon Cho, MD<sup>a</sup>, Sae-Ryung Kang, MD<sup>b</sup>, Seong Young Kwon, MD<sup>b</sup>, Dong-Hyeok Cho, MD, PhD<sup>c</sup>, Jin-Seong Cho, MD, PhD<sup>d</sup>, Ho-Chun Song, MD, PhD<sup>a,\*</sup>

## Abstract

The aim of this study was to evaluate whether the preparation for radioactive iodine (RAI) therapy by thyroid hormone withdrawal (THW) or a low-iodine diet (LID) can be risk factors for the development of hyponatremia in patients with differentiated thyroid cancer after thyroidectomy.

We retrospectively reviewed the medical records and laboratory findings of 326 patients who underwent preparation for RAI therapy after thyroidectomy from 2012 to 2014. Demographic and clinical variables including the method of thyrotropin stimulation and duration of LID were assessed. Serum sodium was measured twice, before operation and before RAI therapy.

Hyponatremia was detected in only 3 patients (0.9%) before operation, but in 15 patients (4.6%) before RAI therapy. None of the patients had severe hyponatremia after preparation for RAI therapy. Pre-RAI therapy serum sodium was correlated with the method of thyrotropin stimulation (THW vs recombinant human thyroid stimulating hormone,  $P=0.014$ ) and duration of LID ( $r=-0.131$ ,  $P=0.018$ ); however, the preparation of RAI therapy, THW and LID, did not affect the development of hyponatremia in logistic regression analysis. Preoperative serum sodium was a significant risk factor for hyponatremia during preparation for RAI therapy.

Preparation for RAI therapy by THW or LID is not a risk factor for the development of hyponatremia in patients with thyroid cancer. The development of hyponatremia was neither frequent nor severe during preparation for RAI therapy. Physicians should not be greatly concerned about rare life-threatening hyponatremia during preparation for RAI therapy.

**Abbreviations:** FT4 = free T4, LID = low-iodine diet, RAI = radioactive iodine, rhTSH = recombinant human thyroid stimulating hormone, T3 = triiodothyronine, T4 = thyroxine, Tg = thyroglobulin, THW = thyroid hormone withdrawal.

**Keywords:** cancer, hyponatremia, low-iodine diet, radioactive iodine therapy, thyroid, thyroid hormone withdrawal

## 1. Introduction

Radioactive iodine (RAI) therapy is a well-established treatment for differentiated thyroid cancer after thyroidectomy. Before RAI therapy or scanning, thyrotropin stimulation and a 2-week low-iodine diet (LID) are required.<sup>[1]</sup> There are case reports

of potentially life-threatening hyponatremia occurring in patients undergoing thyroid hormone withdrawal (THW) and a longer duration of LID.<sup>[2–4]</sup> Restriction of noniodized salt during LID in patients undergoing THW may be associated with hyponatremia.<sup>[5]</sup>

Hyponatremia is the most common electrolyte abnormality in clinical practice.<sup>[6]</sup> It can also be associated with longer hospital stays and higher mortality in patients with cancer.<sup>[7]</sup> Hyponatremia has been reported in patients with noncancer conditions and with various cancer,<sup>[6,8]</sup> but few studies have assessed the frequency and clinical impact in patients with thyroid cancer.<sup>[9,10]</sup> The aim of this study was to evaluate whether the preparation for RAI therapy by THW or LID can be risk factors for development of hyponatremia in patients with differentiated thyroid cancer after thyroidectomy.

## 2. Methods

### 1.1. Patients

We retrospectively studied patients with papillary thyroid carcinoma treated with high dose ( $>1.11$  GBq) I-131 at our institution between 2012 and 2014. Patients who underwent total thyroidectomy with or without dissection of lymph nodes and who had received initial RAI therapy were included. Patients without available medical records or laboratory examinations were excluded. Finally, 326 patients were enrolled in this study. The study was approved by the Institutional Review Board of our hospital.

Editor: Yufang Ma.

*Funding:* This work was supported by the Nuclear Safety Research Program through the Korea Radiation Safety Foundation (KORSAFe) and the Nuclear Safety and Security Commission (NSSC), Republic of Korea (Grant No. 1305033). The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

The authors have no conflicts of interest to disclose.

<sup>a</sup> Department of Nuclear Medicine, Chonnam National University Hospital,

<sup>b</sup> Department of Nuclear Medicine, Chonnam National University Hwasun Hospital, <sup>c</sup> Division of Endocrinology and Metabolism, Department of Internal Medicine, Chonnam National University Hospital, <sup>d</sup> Department of Surgery, Chonnam National University Hospital, Gwangju, Republic of Korea.

\* Correspondence: Ho-Chun Song, Department of Nuclear Medicine, Chonnam National University Hospital and Medical School, Jebongro 42, Donggu, Gwangju 61469, Republic of Korea (e-mail: songhc@chonnam.ac.kr).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2017) 96:5(e6004)

Received: 13 October 2016 / Received in final form: 12 December 2016 /

Accepted: 2 January 2017

<http://dx.doi.org/10.1097/MD.0000000000006004>

**1.2. Study design**

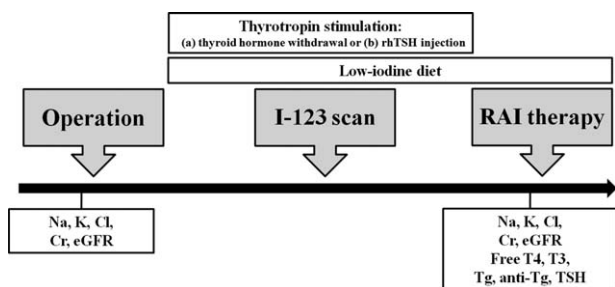
The standard protocol for RAI therapy at our institution is presented in Fig. 1. Initial laboratory examinations for Na, K, Cl, and creatinine were performed the day before the operation. After the operation, the endocrine surgeon referred the patient to the department of nuclear medicine. Diagnostic I-123 whole body scanning was performed to identify appropriate patients for RAI therapy and determine the optimal dose of I-131 after preparation with LID and thyroid stimulating hormone (TSH) elevation. LID is recommended for a 1 to 2 weeks duration, according to major guidelines on this subject.<sup>[1,11,12]</sup> TSH elevation is accomplished by 2 methods: THW, discontinuing levothyroxine (LT4) and changing to liothyronine (LT3) for 2 to 4 weeks followed by withdrawal of LT3 for 2 weeks, or recombinant human TSH (rhTSH, Thyrogen) injection. Patients who meet the criteria for RAI therapy should have an extended period of LID and THW or injection of additional rhTSH. A second laboratory examination for Na, K, Cl, creatinine, free T4 (FT4), T3, thyroglobulin (Tg), antithyroglobulin antibody (anti-Tg), and TSH is performed on the morning of the admission day.

**1.3. Clinical data collection**

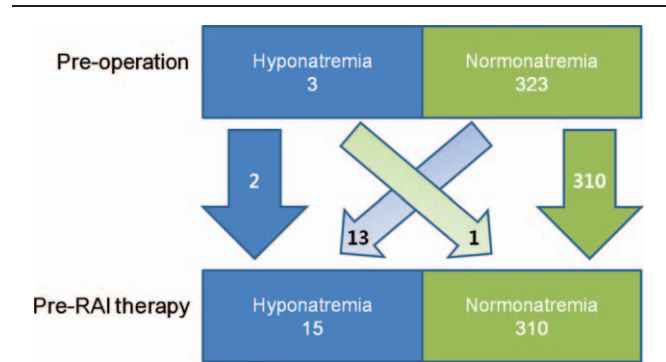
Demographic and clinical variables included the following: age, sex, hypertension (HTN), diabetes mellitus (DM), method of thyrotropin stimulation, duration of LID (days), and laboratory results before operation and before RAI therapy. Reference ranges were: serum Na, 135 to 147mEq/L; K, 3.5 to 5.1 mEq/L; Cl, 98 to 112mEq/L; creatinine, 0.5 to 1.3 mg/dL; FT4, 0.7 to 2 ng/dL; T3, 80 to 220 ng/dL; Tg, 2 to 60 ng/mL; anti-Tg, 0 to 55 U/mL; and TSH, 0.4 to 4.5 μIU/mL. The estimated glomerular filtration rate (eGFR) was calculated according to the simplified Modification of Diet in Renal Disease (MDRD) formula. Hyponatremia was defined as serum sodium (Na) level <135 mEq/L. Serum Na levels were used to classify patients as normonatremic (135–147mEq/L), mildly hyponatremic (130–134mEq/L), moderately hyponatremic (120–129mEq/L), and severely hyponatremic (<120mEq/L).

**1.4. Statistical analysis**

Continuous variables were expressed as the mean ± standard deviation (SD), and categorical variables were expressed as frequencies and percentages. Univariate analysis was performed using Student *t* test for continuous variables and the Chi-square test or Fisher exact test for categorical variables. Correlations between continuous variables for laboratory data were determined based on Pearson correlation coefficient. Logistic regression analyses



**Figure 1.** Protocol for RAI therapy with I-131. Anti-Tg=antithyroglobulin antibody, eGFR=estimated glomerular filtration rate, RAI=radioactive iodine, Tg=thyroglobulin, TSH=thyroid stimulating hormone.



**Figure 2.** The number of patients with hyponatremia and normonatremia. RAI=radioactive iodine.

were performed to evaluate the risk factors for hyponatremia in the preparation for RAI therapy. *P*-value less than 0.05 was considered statistically significant, and statistical analysis was performed using the software SPSS (version 21.0; IBM Corp., Armonk, NY).

**2. Results**

**2.1. Frequency and severity of hyponatremia**

There were only 3 hyponatremic patients (0.9%) before operation, but there were 15 hyponatremic patients (4.6%) before RAI therapy (Fig. 2). After the preparation for RAI therapy, 13 (4.0%) of 323 patients with normonatremic had converted to hyponatremia. None of the patients had hypernatremia.

Before operation, there were 2 patients with mild hyponatremia (133 and 134 mEq/L) and 1 with moderate hyponatremia (127 mEq/L), whereas before RAI therapy, there were 14 with mild hyponatremia (134.1 ± 1.1 mEq/L) and 1 with moderate hyponatremia (125 mEq/L). Most patients with hyponatremia had only a mild degree after preparation for RAI therapy. None had severe hyponatremia.

**2.2. Comparison of hyponatremic and normonatremic groups**

Before operation, the mean serum levels of Na and Cl were lower in the hyponatremia group than in the normonatremia group; however, there were no differences in age, sex, HTN, DM, serum K, blood urea nitrogen (BUN), creatinine or eGFR between the 2 groups (Table 1). However, before RAI therapy, the percentage of DM patients was higher in the hyponatremia group (27%) than in the normonatremia group (6%). The mean level of preoperative Na was lower in the hyponatremia group. There were no differences in age, sex, HTN, duration of LID, method of thyrotropin stimulation, preoperative K, Cl, creatinine and eGFR, or pre-RAI therapy FT4, T3, Tg, anti-Tg, or TSH.

**2.3. Factors associated with serum Na before RAI therapy**

As shown in Table 2, for the continuous variables, pre-RAI therapy serum Na level was correlated with patient age ( $r = 0.129, P = 0.019$ ), duration of LID ( $r = -0.131, P = 0.018$ ) and preoperative Na level ( $r = 0.391, P < 0.001$ ). However, pre-RAI therapy serum Na level was not correlated with preoperative K, Cl, creatinine, and eGFR, or pre-RAI therapy FT4, T3, Tg, anti-Tg, or TSH.

**Table 1**  
**Baseline characteristics.**

	Before operation			Before RAI therapy		
	Hyponatremia (N=3)	Normonatremia (N=323)	P	Hyponatremia (N=15)	Normonatremia (N=311)	P
Age, y	60.0±14.7	49.5±12.4	0.148	55.8±15.9	49.3±12.3	0.140
Sex, female	3 (100%)	256 (79%)	1.000	11 (73%)	248 (80%)	0.520
HTN, yes	1 (33%)	70 (22%)	0.523	6 (40%)	65 (21%)	0.105
DM, yes	0 (0%)	23 (7%)	1.000	4 (27%)	19 (6%)	0.015
Method of thyrotropin stimulation, THW	1 (33%)	94 (29%)	1.000	11 (73%)	220 (71%)	1.000
Duration of LID, d	24.3±2.9	21.1±5.3	0.297	21.0±5.1	24.0±7.8	0.166
Preoperative Na, mEq/L	131.3±3.8	140.1±2.0	<0.001	138.0±3.7	140.1±2.0	0.047
Preoperative K, mEq/L	4.3±0.4	4.2±2.0	0.906	4.3±0.6	4.2±2.1	0.911
Preoperative Cl, mEq/L	95.3±3.5	103.0±6.1	0.031	101.9±4.3	103.0±6.2	0.477
Preoperative creatinine, mg/dL	0.6±0.1	0.8±0.8	0.756	1.37±2.7	0.7±0.6	0.375
Preoperative eGFR, mL/min/1.73 m <sup>2</sup>	105.3±24.5	102.2±26.7	0.840	98.1±36.5	102.4±26.1	0.535
Pre-RAI therapy free T4, ng/dL	—	—	—	1.2±0.2	1.3±0.3	0.728
Pre-RAI therapy T3, ng/dL	—	—	—	105.4±25.0	108.7±24.0	0.704
Pre-RAI therapy Tg, ng/mL	—	—	—	103.1±174.8	35.5±71.8	0.281
Pre-RAI therapy anti-Tg, U/mL	—	—	—	30.8±14.4	77.3±559.8	0.804
Pre-RAI therapy TSH, $\mu$ IU/mL	—	—	—	2.1±1.3	2.0±1.5	0.878

Anti-Tg = antithyroglobulin antibody, DM = diabetes mellitus, eGFR = estimated glomerular filtration rate, HTN = hypertension, LID = low-iodine diet, RAI = radioactive iodine, Tg = thyroglobulin, THW = thyroid hormone withdrawal, TSH = thyroid stimulating hormone.

For the categorical variables, the method of thyrotropin stimulation and DM were associated with the change in serum Na level. Serum Na level was decreased significantly more in the THW group than in the rhTSH group (Fig. 3A,  $P=0.014$ ), and serum Na level decreased significantly more in the DM group than in the non-DM group (Fig. 3B,  $P=0.059$ ). However, sex (Fig. 3C) and HTN (Fig. 3D) were not associated with a change in serum Na level.

Logistic regression analyses were performed to evaluate factors associated with hyponatremia before RAI therapy (Table 3). Preoperative serum Na was the only significant factor associated with pre-RAI therapy hyponatremia (continuous variable;  $P=0.001$ , odds ratio [OR]: 0.674; 95% confidence interval [CI], 0.538–0.846, hyponatremia;  $P=0.001$ , OR: 61.096; 95% CI, 4.971–750.945). Age (continuous variable;  $P=0.064$ , old age over 60 years;  $P=0.068$ ), DM ( $P=0.057$ ), and duration of LID (continuous variable;  $P=0.063$ ) showed borderline  $P$  values. However, the preparation for RAI therapy of THW and 2-week LID commonly recommended duration according to most guidelines did not affect the development of hyponatremia.

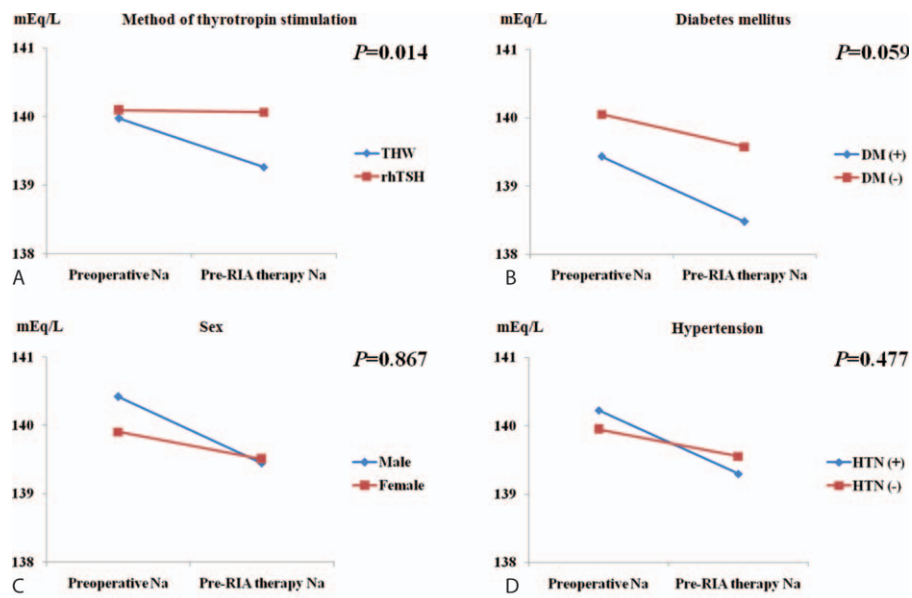
**Table 2**  
**Factors associated with pre-RAI therapy serum Na level.**

	Pearson correlation $r$	Significance $P$
Age, y	0.129	0.019
Duration of LID, d	-0.131	0.018
Preoperative Na, mEq/L	0.391	<0.001
Preoperative K, mEq/L	0.000	1.000
Preoperative Cl, mEq/L	0.056	0.309
Preoperative creatinine, mg/dL	-0.079	0.156
Preoperative eGFR, mL/min/1.73 m <sup>2</sup>	-0.051	0.359
Pre-RAI therapy free T4, ng/dL	0.128	0.059
Pre-RAI therapy T3, ng/dL	-0.006	0.926
Pre-RAI therapy Tg, ng/mL	-0.112	0.097
Pre-RAI therapy anti-Tg, U/mL	-0.059	0.386
Pre-RAI therapy TSH, $\mu$ IU/mL	-0.054	0.427

Anti-Tg = antithyroglobulin antibody, eGFR = estimated glomerular filtration rate, LID = low-iodine diet, RAI = radioactive iodine, Tg = thyroglobulin, TSH = thyroid stimulating hormone

### 3. Discussion

In the present study, we demonstrated that preparation for RAI therapy using THW and LID did not cause frequent or severe hyponatremia. Hyponatremia was only present in 3 cases (<1%) before operation, and in 15 cases (4.6%) before RAI therapy. After preparation for RAI therapy, there was only a 3.7% increase in hyponatremic patients. The hyponatremia rate in this study was lower than that obtained in previous reports. Doshi et al<sup>[6]</sup> reported that the hyponatremia rate in patients with cancer admitted for the first time to the hospital was 47%. Such differences in the hyponatremia rate are attributable to the patients' characteristics. Our study only included cases with thyroid papillary carcinoma, which is a less aggressive malignancy and younger patients (mean, 50±12 years) than those studied by Doshi et al (mean, 56±17 years) might be associated with the lower rate of hyponatremia. Another major finding was that none of the subjects showed severe hyponatremia after preparation for RAI therapy. Our study had only 1 patient with moderate hyponatremia with a serum Na level of 125 mEq/L. She had no symptoms suggesting hyponatremia and her hyponatremia became normalized after administration of an oral sodium chloride tablet. Our results correspond well to previous studies of patients undergoing preparation for RAI therapy. Baajafer et al<sup>[13]</sup> showed that of 120 patients who were prepared for RAI therapy using both THW and LID, none had serum sodium values below 130 mEq/L. There were several case reports of moderate to severe hyponatremia after preparation for RAI therapy in patients with other contributing factors such as old age, thiazide use, etc.<sup>[3,4]</sup> Hyponatremia is frequent in patients with or without cancer admitted to the hospital, but is rare in patients with thyroid cancer admitted to the hospital. Severe hyponatremia can induce fatal complications, but there were no cases with severe hyponatremia during the preparation for RAI therapy and hyponatremic patients were successfully treated by sodium chloride tablets. Therefore, preparation for RAI therapy using THW or LID appears to be a safe procedure, and does not need intensive monitoring in patients with thyroid cancer.



**Figure 3.** Factors associated with a change in serum sodium level. Serum sodium levels in the thyroid hormone withdrawal (THW) group decreased markedly, but levels in the recombinant human TSH (rhTSH) group showed little change. Serum Na level decreased more in the THW group than in the rhTSH group (A). Serum sodium level decreased more in diabetic patients than in nondiabetic patients (B). The change in serum sodium level did not show any differences according to sex (C) or presence of hypertension (D).

Our results also showed that preparation for RAI therapy with THW or LID was not a risk factor for the development of hyponatremia in patients with thyroid cancer. Hypothyroidism induced by THW has been considered a major contributing factor for the development of hyponatremia.<sup>[10,14]</sup> Hypothyroid patients have a diminished ability to excrete free water, fail to achieve maximum urine dilution, and show delayed excretion of a water load leading to hyponatremia.<sup>[15]</sup> Our study showed that patients with hypothyroidism induced by THW had a lower serum Na level before RAI therapy than euthyroid patients who received rhTSH injection, even with similar serum Na levels

before operation. Low sodium intake along with LID might be additional contributing factors for the development of hyponatremia in patients with thyroid cancer.<sup>[13,14]</sup> Severe restriction of sodium intake often occurs during the LID period despite the availability of iodine-free salt.<sup>[4]</sup> The deficit of sodium induces hyponatremia. Our study also showed that there was an inverse correlation between the duration of LID and serum Na level before RAI therapy; the longer the duration of LID, the lower the serum Na level. Our results demonstrated that a hypothyroid state and prolonged LID duration were significantly correlated with serum Na level before RAI therapy. However, THW and 2-week LID, which is the most commonly recommended duration from authoritative guidelines, were not risk factors for the development of hyponatremia in the logistic regression analysis. Other patients who reported the development of hyponatremia during preparation for RAI therapy also had contributing cofactors such as old age, thiazide use, and other comorbidities making them more prone to hyponatremia.<sup>[5]</sup> This suggests that THW and LID could induce a somewhat low serum Na level, and excessive longer LID duration might increase the possibility of hyponatremia. However, THW or LID per se could not be a strong risk factor for the development of significant hyponatremia, because following the current recommendations for LID duration was not associated with a higher risk of hyponatremia. Thus, nuclear medicine physicians should consider causes other than THW or LID when patients have pre-RAI therapy hyponatremia.

Another major finding was that preoperative serum Na level was the only risk factor for the development of hyponatremia before RAI therapy. Among the hyponatremic patients before operation, 2 of 3 remained hyponatremic after preparation for RAI therapy. Moreover, increased fluid intake of over 2 L daily is recommended during hospitalization to promote excretion of residual RAI in the isolation room.<sup>[16]</sup> Excessive oral hydration may potentiate an electrolyte imbalance and thus contribute to the development of hyponatremia in high risk patients.<sup>[2]</sup>

**Table 3**

**Logistic regression analysis of factors associated with the development of hyponatremia before RAI therapy.**

	P	Exp (B)	95% CI
Method of thyrotropin stimulation			
rhTSH	Ref		
THW	0.533	2.407	0.152–38.167
Duration of LID			
Continuous, days	0.063	1.261	0.987–1.611
<14 days	Ref		
≥14 days	0.835	0.737	0.042–13.081
Age			
Continuous, years	0.064	1.046	0.997–1.097
<60 years	Ref		
≥60 years	0.068	3.146	0.919–10.766
DM			
No	Ref		
Yes	0.057	3.870	0.959–15.612
Preoperative Na			
Continuous, mEq/L	0.001	0.662	0.522–0.840
Normonatremia (≥135 mEq/L)	Ref		
Hyponatremia (<135 mEq/L)	0.001	61.096	4.971–750.945

CI=confidence interval, DM=diabetes mellitus, LID=low-iodine diet, RAI=radioactive iodine, rhTSH=recombinant human thyroid stimulating hormone, THW=thyroid hormone withdrawal.



Therefore, patients who have lower preoperative serum Na levels should be monitored during the preparation for RAI therapy.

This study has several limitations. First, it is limited by its retrospective design and by the relatively small number of patients enrolled; thus its prediction power is relatively low. Further prospective studies including more patients with hyponatremia are therefore necessary. Second, serum and urine osmolality tests or hormone assays were not evaluated to further investigate the causes of hyponatremia in this study. However, none of the patients had severe or symptomatic hyponatremia, and further examination was not essential before RAI therapy.

#### 4. Conclusion

Preparation for RAI therapy using THW or LID is not a risk factor for the development of hyponatremia in patients with thyroid cancer. Hyponatremia was neither frequent nor severe during preparation for RAI therapy when developed. Physicians need not be greatly concerned about rare, life-threatening hyponatremia during preparation for RAI therapy, and should not overestimate the possibility of the development of severe hyponatremia.

#### References

- [1] Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: the American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016;26:1–33.
- [2] Kim SK, Yun GY, Kim KH, et al. Severe hyponatremia following radioactive iodine therapy in patients with differentiated thyroid cancer. *Thyroid* 2014;24:773–7.
- [3] Krishnamurthy VR, McDougall IR. Severe hyponatremia: a danger of low-iodine diet. *Thyroid* 2007;17:889–92.
- [4] Shakir MK, Krook LS, Schraml FV, et al. Symptomatic hyponatremia in association with a low-iodine diet and levothyroxine withdrawal prior to I131 in patients with metastatic thyroid carcinoma. *Thyroid* 2008;18:787–92.
- [5] Al Nozha OM, Vautour L, How J. Life-threatening hyponatremia following a low-iodine diet: a case report and review of all reported cases. *Endocr Pract* 2011;17:e113–7.
- [6] Doshi SM, Shah P, Lei X, et al. Hyponatremia in hospitalized cancer patients and its impact on clinical outcomes. *Am J Kidney Dis* 2012;59:222–8.
- [7] Upadhyay A, Jaber BL, Madias NE. Epidemiology of hyponatremia. *Semin Nephrol* 2009;29:227–38.
- [8] Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. *Am J Med* 2006;119(7 suppl 1):S30–5.
- [9] Hammami MM, Almogbel F, Hammami S, et al. Acute severe hypothyroidism is not associated with hyponatremia even with increased water intake: a prospective study in thyroid cancer patients. *BMC Endocr Disord* 2013;13: DOI: 10.1186/1472-6823-13-27.
- [10] Lee JE, Kim SK, Han KH, et al. Risk factors for developing hyponatremia in thyroid cancer patients undergoing radioactive iodine therapy. *PLoS ONE* 2014;9:e106840.
- [11] Luster M, Clarke SE, Dietlein M, et al. Guidelines for radioiodine therapy of differentiated thyroid cancer. *Eur J Nucl Med Mol Imaging* 2008;35:1941–59.
- [12] Yi KH, Park YJ, Koong SS, et al. Revised Korean Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Thyroid Cancer. *Int J Thyroidol* 2010;3:65–96.
- [13] Baajafer FS, Hammami MM, Mohamed GE. Prevalence and severity of hyponatremia and hypercreatininemia in short-term uncomplicated hypothyroidism. *J Endocrinol Invest* 1999;22:35–9.
- [14] Nozu T, Yoshida Y, Ohira M, et al. Severe hyponatremia in association with I(131) therapy in a patient with metastatic thyroid cancer. *Intern Med* 2011;50:2169–74.
- [15] Hanna FW, Scanlon MF. Hyponatraemia, hypothyroidism, and role of arginine-vasopressin. *Lancet* 1997;350:755–6.
- [16] Sisson JC, Freitas J, et al. American Thyroid Association Taskforce on Radioiodine Safety Radiation safety in the treatment of patients with thyroid diseases by radioiodine 131I: practice recommendations of the American Thyroid Association. *Thyroid* 2011;21:335–46.