Inaccuracy of Thyroid to Background Uptake Ratio in Evaluating Technetium-99m-pertechnetate Thyroid Uptake and Establishing an Improved Algorithm

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Objective(s): The aim of this study was to explore the accuracy of thyroid to background uptake ratio (UR) in the evaluation of 99mTc-pertechnetate thyroid uptake (TcTU) and establishment of an improved algorithm.

Methods: This study was conducted on the thyroid images of 322 patients with thyroid diseases and 67 controls. For the purpose of the study, URs of the images were calculated, and then corrected by standardized thyroid area size to establish a corrected uptake ratio (CUR). Subsequently, the accuracy between UR and CUR was compared.

Results: The results of linear regression using weighted least squares (using TcTU as a dependent variable and CUR, UR, or thyroid area size as independent variables) showed that CUR (t=105.5, P=0.000), UR (t=31.9, P=0.000), and thyroid area size (t=15.9, P=0.000) are influential factors of TcTU. Furthermore, the standardized coefficient of CUR (β=0.983) was obviously higher than those of UR (β=0.851) and thyroid area size (β=0.629). The linear goodness-of-fit between CUR and TcTU (R=0.983) was better than that between UR and TcTU (R=0.851). In addition, the total concordance rate between CUR and TcTU (96.7%) was significantly higher than that between UR and TcTU (83.0%; χ²=42.9, P=0.000). Discordance rates of CUR in large thyroid area (1.4% vs. 13.4%, χ²=17.0, P=0.000) and small thyroid area (3.3% vs. 42.2%, χ²=44.3, P=0.000), were significantly lower than that of UR. In the abnormal thyroid areas, the discordance rates of UR obviously increased as compared to those of CUR. The UR overestimated the thyroid uptake in small thyroid areas and underestimated it in large thyroid areas.

Conclusion: Based on the findings, CUR is more accurate than UR in measuring 99mTcO₂⁺ thyroid uptake; accordingly, it is more significant in the diagnosis of thyroid disease.

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**Introduction**

$^{99m}$Tc-pertechnetate thyroid uptake (TcTU) rate is a quantitative parameter used for various medical purposes, such as diagnosis (1-3), differential diagnosis (4), and evaluation of the therapeutic effects (5-7) of thyroid diseases. The TcTU is an accurate method in evaluating $^{99m}$TcO$_4^−$ thyroid uptake; however, this method is not widely used in clinical practices due to its relative complexity.

Many semiquantitative methods, such as thyroid to thigh uptake ratio (8-10), thyroid to salivary ratio (11-14), thyroid to right upper lung ratio (15), thyroid to neck ratio (16), thyroid to mediastinum ratio, and thyroid to brain ratio, are more convenient than TcTU and are widely used to indirectly measure $^{99m}$TcO$_4^−$ thyroid uptake. However, these ratios are not always consistent with their TcTU values. Zhang et al. (16) reported contradictory results by observing high ratios of thyroid to background but normal TcTU values in some patients with subtotal or partial thyroidectomy. The present study involved a clinically similar situation to that of Zhang.

This study targeted toward proposing a new ratio algorithm. The new ratio method is more accurate than the above-mentioned ratio methods, and its accuracy is very similar to that of TcTU.

**Methods**

**Study population**

The study protocols were approved by the Ethics Committees of Zhongnan Hospital of Wuhan University, Hubei, China (No. 2014065); furthermore, informed consent was obtained from all individuals. This study was conducted on 389 individuals undergoing thyroid imaging and TcTU measurement, including 67 controls (i.e., 16 males and 51 females; age range: 20-63 years, mean age: 38.5±10.6 years) and 322 patients with definite thyroid disease (i.e., 68 males and 254 females; age range: 18-71 years, mean age: 41.7±14.2 years).

The thyroid patients consisted of 79 cases with Graves hyperthyroidism, 40 cases with simple goiter, 28 cases with subacute thyroiditis, 41 cases with hypothyroidism, 23 euthyroid patients of postoperation of Graves hyperthyroidism, 44 postoperative patients of thyroid nodules, 48 cases with thyroid nodules and 19 cases with Hashimoto's disease. There was no toxic nodular goiter case in the Graves’ hypothyroidism and thyroid nodule groups. The patients in the hypothryoidism group had no determinable thyroid nodule. If the patients with hypothyroidism had a determinable nodule, they entered into the thyroid nodule group. The diagnosis of thyroid diseases accorded with the relevant guidelines (17, 18).

The individuals in the control group, who were initially suspected of having thyroid diseases, were finally confirmed to have no thyroid disease by clinical palpation, examination of color Doppler ultrasound, and laboratory examinations. According to our routine requirement, none of the patients had taken iodine-containing drugs, such as cydiodine buccal tablets 2 weeks before thyroid imaging and TcTU measurements (19).

**Grouping of individuals**

In this study, TcTU was accepted as a standard method for evaluating $^{99m}$TcO$_4^−$ thyroid uptake. The thyroid to background uptake ratio (UR) is a semiquantitative parameter. We analyzed the distribution of discordance rate between the UR and TcTU results in determining the reduction, normality, or elevation of $^{99m}$TcO$_4^−$ thyroid uptake. It was found that the discordance of UR was related to the thyroid area size and presented mainly under the condition of abnormal size of the thyroid area. For the purpose of the study, UR was corrected based on the average thyroid area size of the control group. Subsequently, the corrected uptake ratio (CUR) of thyroid to background and UR were compared in terms of accuracy.

To analyze the discordance distribution and discordance type of UR, the individuals enrolled in this study were assigned into three groups according to the thyroid area size. The three groups included small thyroid area (thyroid area<16.5 cm$^2$; n=90), normal thyroid area (16.5 cm$^2$≤thyroid area size≤27.6 cm$^2$; n=157), large thyroid area (thyroid area size>27.6 cm$^2$; n=142).

To calculate the concordance rates between UR (or CUR) and TcTU and the discordance rates of UR and CUR in different thyroid sizes and uptakes and compare the accuracy between UR and CUR, the individuals were also divided into three groups according to TcTU, UR, and CUR. These groups included decreased thyroid uptake (TcTU, UR, or CUR values ≤lower limits of reference ranges), normal thyroid uptake (lower limits of reference ranges ≤TcTU, UR, or CUR values ≤ upper limits of reference ranges), and increased thyroid uptake (TcTU, UR, or CUR values >upper limits...
of reference ranges). The reference ranges of the above-mentioned parameters are presented in the result section.

**Imaging method**

Gamma camera with a low-energy and high-resolution collimator (e-CAM; Siemens product, Hoffman Estates, Illinois, USA), dose calibrator (FT-3106; Shanghai Electronic Instrument Factory, China), and 99Mo-99mTc generator (Beijing Transtech Services, China) were used in this study. The calibration factor between the radioactivity intensity, measured with a dose calibrator, and the radioactivity counts, measured by a gamma camera, were calculated according to the manual provided by the gamma camera manufacturer.

The radioactivity of syringe containing radiopharmaceutical were separately measured by means of the dose calibrator before and after the intravenous injection of Na99mTcO₄ of 74-185 MBq. Twenty minutes after the intravenous injection of Na99mTcO₄, thyroid imaging was performed while placing the patients in a supine position with the head hyperextended using a horizontal detector with a matrix of 256×256 and zoom of 3.2 taking 5 min. After the completion of thyroid imaging, the injection site was examined. If the injection leakage was visible in the monitor, a leakage imaging was performed for 1 min using a matrix of 256×256 and zoom of 1.0.

**Image processing and region of interest (ROI) drawing**

Thyroid images were displayed with a spectrum scale and a gamma parameter of 1.0. The contrast and brightness were adjusted to clearly show the edge of the thyroid tissue without altering the image size. The thyroid region of interest (ROI) was then outlined along the edge of the thyroid tissue while only surrounding the thyroid tissue with 99mTcO₄⁻ uptake. The background ROI was outlined under the thyroid glands (Figure 1).

**Calculation of quantitative and semiquantitative parameters**

Table 1 presents the formulæ and parameters for calculating UR, CUR, and TcTU. The schematic representation of this procedure is also depicted in Figure 2. The specific algorithm of TcTU is given in the supplementary file 1. In these calculations, the average thyroid area of the control group was regarded as a reference standard. Then, the radioactivity counts in the thyroid ROI was converted into the radioactivity counts of the standardized size of thyroid (C₉). In addition, the radioactivity counts in the background ROI was converted into the counts in the standardized size of background (C₉).

**Statistical analysis**

The data were analyzed in SPSS statistical software (version 22.0; IBM Corporation, Armonk, New York, USA). The data are depicted in a scatterplot and listed in tables using median and interquartile range (IQR). Linear regression analysis by weighted least squares was used to evaluate the linear relationships between $S_S$ and TcTU, between UR and TcTU, and between CUR and TcTU. In addition, the analysis of variance was adopted to determine the significance of the linear model. The significance of regression coefficients was also investigated by means of the t-test. Furthermore, the Chi-square test was performed to compare the difference in rates. Mann-Whitney U test as a nonparametric test was also used to compare the thyroid and control groups in terms of $S_S$, TcTU, UR, and CUR. P-value less than 0.05 was considered statistically significant.

**Results**

**Reference ranges of TcTU, UR, CUR, and $S_S$**

The mean TcTU, UR, CUR, and thyroid area size (cm²) were 2.17±0.69, 4.23±0.92, 4.17±0.93, and 22.06±2.82, respectively. The reference ranges were calculated at 95% confidence interval (mean±1.96SD). The reference ranges of TcTU (%), UR, CUR, and thyroid area size (cm²) were 0.82-3.52, 2.43-6.03, 2.35-5.99, and 16.5-27.6, respectively.
Comparison of UR among thyroid and control groups

The results of UR in patients with different thyroid diseases and control group are listed in Table 2. The results revealed that the UR of the Graves’ hyperthyroidism group was significantly higher than that of the control group (P<0.05). On the other hand, the URs of the patients with subacute thyroiditis, hypothyroidism, and postoperative thyroid nodule were significantly lower than that of the control group (P<0.05).

In the four diseases, UR was similar to TcTU (Supplementary Table 1) in determining the thyroid uptake. The simple goiter and Hashimoto’s disease groups showed no significant difference with the control group in terms of UR (P>0.05), which is different from their TcTU. In this respect, the TcTU was higher in the simple goiter and Hashimoto’s disease groups than in the control group (Supplementary Table 1).

The UR of the euthyroid patients after surgery for Graves’ hyperthyroidism was significantly higher than that of the control group (P<0.05). On the other hand, the TcTU of this group was similar to TcTU.
significantly lower than that of the control group (Supplementary Table 1). Furthermore, the UR of the thyroid nodule group was significantly lower than that of the control group (P<0.05). However, there was no significant difference between these groups in TcTU (Supplementary Table 1). Therefore, UR obviously differed from TcTU in determining \(^{99m}\text{TcO}_4^-\) thyroid uptake.

**Comparison of CUR among thyroid and control groups**

Table 3 summarizes the CUR results of patients with different thyroid diseases and control group.

As the results indicated, the CURs of Graves’s hyperthyroidism, simple goiter, and Hashimoto’s disease groups were significantly higher than that of the control group (P<0.05). On the other hand, the CUR of subacute thyroiditis, Graves’ hypothyroidism, and postoperative thyroid nodule were significantly lower than that of the control group (P<0.05). The difference of CUR between the thyroid nodule and control groups was not statistically significant (P>0.05).

In the seven diseases, CUR was similar to TcTU in determining pertechnetate thyroid uptake (Supplementary Table 1). The difference
between the patients developing euthyroidism after surgery for hyperthyroidism and control groups was not significant in terms of CUR (P>0.05). However, TcTU was significantly lower in the euthyroid patients (occurring after hyperthyroidism operation) in comparison to that in the control group (Supplementary Table 1). Both CUR and TcTU were mostly in the normal range in this group and in line with their thyroid hormone level. In total, CUR was very similar to TcTU in determining 99mTcO4− thyroid uptake.

**Concordance rates between UR and TcTU and between CUR and TcTU**

Table 4 presents the concordance rate between UR and TcTU and between CUR and TcTU in different thyroid sizes. The results showed that the concordance rate between UR and TcTU in small thyroid area was obviously lower than that in the large thyroid area (χ²=24.4, P=0.000). Furthermore, the concordance rate in large thyroid areas was significantly lower than that in normal thyroid area size (χ²=5.21, P=0.022). Therefore, in small thyroid areas, UR and TcTU had the lowest concordance rate. However, in different thyroid area sizes, the concordance rates between CUR and TcTU did not present a significant difference (χ²=3.38, P=0.184). In the abnormal thyroid area size, the concordance rates between CUR and TcTU were significantly higher than that between UR and TcTU (P<0.05; Table 4).

**Distribution of discordant UR results and comparison of discordance rate between UR and CUR**

Supplementary Table 2 lists the discordance rates of UR and CUR in different thyroid area sizes. According to the results, the discordant results of UR were mainly distributed in the small and large thyroid areas. The results showed that the UR discordance types were diverse. In the small thyroid areas, many patients with decreased TcTU were wrongly determined as normal 99mTcO4− uptake by UR (Figure 3, Supplementary Figure 1), and many patients with normal TcTU were wrongly determined as high 99mTcO4− uptake by UR (Figure 4).

Furthermore, in the large thyroid areas, some patients with increased TcTU were wrongly
determined as normal $^{99m}$TcO$_4^-$ uptake by UR, and some patients with normal TcTU were decided as low $^{99m}$TcO$_4^-$ uptake by UR. Under these conditions (i.e., small and large thyroid areas), the UR discordance rates were significantly higher than those of CUR ($P<0.05$). Nonetheless, in the normal thyroid area size, there was no significant difference between the CUR and UR in terms of the discordance rate ($P>0.05$).

**Comparison of the linear relationship between UR to TcTU and CUR to TcTU**

In order to explore the relationship between thyroid area size and TcTU and compare the linear relationship between UR to TcTU and CUR to TcTU, linear regression analyses by weighted least squares were performed between thyroid area size and TcTU, between UR and TcTU, and between CUR and TcTU. The results of regression analyses
Table 5. Goodness-of-fit of \( S_t \) to TcTU, UR to TcTU, and CUR to TcTU in a linear regression model using weighted least squares

| Dependent variable | Independent variable | R     | Adjusted R square | Coefficients | b      | Std. error of b | \( \beta \) | t   | P-value |
|--------------------|----------------------|-------|-------------------|--------------|-------|-----------------|--------|-----|---------|
| TcTU               | \( S_t \)            | 0.629 | 0.394             |              | 0.143 | 0.009           | 0.629  | 15.93| 0.000   |
|                    | Constant             |       |                   |              | -0.330| 0.037           | -8.87  | 0.000|         |
| TcTU               | UR                   | 0.851 | 0.724             |              | 0.765 | 0.024           | 0.851  | 31.90| 0.000   |
|                    | Constant             |       |                   |              | -0.926| 0.049           | -18.74 | 0.000|         |
| TcTU               | \( S_t \)            | 0.094 | 0.799             |              | 0.708 | 0.021           | 0.788  | 33.74| 0.000   |
|                    | Constant             |       |                   |              | 0.024 | 0.002           | 0.282  | 12.09| 0.000   |
| TcTU               | UR*\( S_t \)         | 0.982 | 0.964             |              | 0.028 | 0.000           | 0.982  | 102.61| 0.000   |
|                    | Constant             |       |                   |              | -0.294| 0.020           | -14.49 | 0.000|         |
| TcTU               | \( S_t \)            | 0.983 | 0.966             |              | 0.680 | 0.006           | 0.983  | 105.52| 0.000   |
|                    | Constant             |       |                   |              | -0.738| 0.017           | -44.20 | 0.000|         |
| TcTU               | UR                   | 0.975 | 0.952             |              | 0.001 | 0.021           | 0.001  | 0.06 | 0.955   |
|                    | Constant             |       |                   |              | -0.711| 0.021           | -33.27 | 0.000|         |
| TcTU               | \( S_t \)            | 0.983 | 0.966             |              | 0.685 | 0.007           | 0.990  | 94.12| 0.000   |
|                    | Constant             |       |                   |              | -0.002| 0.001           | -0.015 | 0.82 | 0.146   |

TcTU: \(^{99m}\)Tc-pertechnetate thyroid uptake rate, UR: thyroid to background uptake ratio, CUR: corrected UR, \( S_t \): thyroid area size, \( R \): multiple correlation coefficient, \( R \) square: coefficient of determination, \( b \): unstandardized regression coefficient, \( \beta \): standardized regression coefficient.

are presented in Table 5. The regression showed that thyroid area size and TcTU were linearly related (F=253.6, P=0.000), and 39.4% variation of TcTU could be interpreted by the thyroid area size. Linear regression also showed that UR and \( S_t \) presented a significant interaction.

The UR*\( S_t \) is an interaction variable, and CUR is another type of the interaction variable. The results revealed CUR, UR, and thyroid area size as the influential factors of TcTU, respectively. However, when the UR and \( S_t \) were separately entered into the linear model, together with CUR, the variables of UR and \( S_t \) were not statistically significant (P>0.05). This indicates that CUR is a decisive factor as compared to the UR and \( S_t \).

As displayed in Figure 5, both CUR to TcTU and
UR to TcTU presented a linear tendency. In Figure 5A, the points of UR to TcTU were distanced; however, in Figure 5B, the points of CUR to TcTU were very close. It was thus clear that the linearity of CUR to TcTU was better than that of UR to TcTU. The regression results confirmed that both UR to TcTU (F=1017.3, P=0.000) and CUR to TcTU (F=11134.5, P=0.000) were linearly related. The linear goodness-of-fit parameters of CUR to TcTU were higher than those of UR to TcTU (Table 5). According to the results, the correlativity between CUR and TcTU was obviously better than that between UR and TcTU.

Discussion

Usefulness and limitations of UR

The TcTU as an important quantitative parameter (20) and UR as a semiquantitative parameter, are the measurement methods of 99mTcO4− thyroid uptake. In this study, the reference range of TcTU was obtained at 0.82-3.52%, which is similar to the ranges reported by Prakash (1.0-4.0%) in India (21), Zhang et al. (0.48-3.68%) in China (16), and Shigemasa et al. (0.7-3.0%) in Japan (22). However, it is markedly different from the reference range (0.35-1.7%) reported by Ramos et al. (23) and Zantut-Wittmann et al. (24) in Brazil.

As indicated in the literature, the normal values of TcTU depend on the applied technique and dietary intake of iodide (8, 9). Therefore, each laboratory should establish its normal values. Zhang et al. (16) reported a strong correlation between semiquantitative ratio and TcTU (r=0.82, P<0.01). Given the simplicity of semiquantitative ratio, many different ratio methods are widely used for the evaluation of 99mTcO4− thyroid uptake. The UR of this study is similar to the other semiquantitative ratios.

Our results showed a linear relationship between UR and TcTU; furthermore, the total concordance rate between UR and TcTU was estimated at 83.0%, which is similar to the results reported in the literature (16). Therefore, UR can be used to estimate the 99mTcO4− thyroid uptake of patients to some extents and is of important clinical value. Despite its wide application, UR still has some shortcomings. Zhang et al. (16) found a discrepancy between UR and TcTU. Our study supported the viewpoint of Zhang et al. Under the condition of small thyroid area, 39.0% of the patients with decreased TcTU were wrongly determined to have a normal uptake of 99mTcO4− (Supplementary Table 2, Figure 3, Supplementary Figure 1). In addition, 51.7% of the patients with normal TcTU were wrongly determined to have a high uptake of 99mTcO4− (Figure 4, Supplementary Table 2), which showed that the quantity of 99mTcO4− thyroid uptake was overestimated by UR.

Under the condition of large thyroid area, 15.7% of the patients with increased TcTU were wrongly determined to have a normal uptake of 99mTcO4−, and 12.0% of the patients with normal TcTU were wrongly determined to have a low uptake of 99mTcO4− (Supplementary Table 2), which manifested that the quantity of 99mTcO4− thyroid uptake was underestimated by UR. Therefore, UR presented much discordance under an abnormal thyroid size and could not completely replace TcTU.

Why does UR present more discordance?

The linear relationship between thyroid area size and TcTU indicated that the change of TcTU depends on the thyroid area size. Accordingly, the partial variations of TcTU may be explained by the change of the thyroid area size. Regarding this, thyroid area size is a factor influencing the accuracy of measuring 99mTcO4− thyroid uptake by ratio methods. Changes in thyroid area size are common in patients with thyroid disease and after treatment for thyroid diseases (Supplementary Table 3).

The UR is a relative ratio between the radioactivity in the thyroid and that in the background without a unit of measurement, which indicates that the relative uptake value does not include any information regarding the thyroid area size. Our findings demonstrated that the quantity of 99mTcO4− thyroid uptake was affected by not only UR but also thyroid area size. Under an invariable UR condition, a bigger thyroid area size is accompanied by a higher quantity of 99mTcO4− thyroid uptake. Based on this analysis, UR could not always accurately reflect the alteration of 99mTcO4− thyroid uptake when disregarding the thyroid area size.

After thyroidectomy, the area size of the residual thyroid tissues frequently becomes smaller and their UR could be similar to or higher than the preoperative UR given the influence of increased thyroid stimulating hormone. However, their absolute uptake of 99mTcO4− after thyroidectomy is lower than that before thyroidectomy, resulting in occasional inconsistencies between UR and TcTU (Figure 4, Supplementary Figure 1).

For subacute thyroiditis, under the condition of partial thyroid tissue imaging, the UR sometimes does not agree with TcTU (Figure 3). Meanwhile,
our results showed that UR also had some discordance under a large thyroid area (13.4%). These phenomena demonstrate that the non-consideration of thyroid area size is the main reason for the high discordance of UR under an abnormal thyroid area size.

**Methodological features of CUR**

Considering that the accuracy of UR in deciding thyroid uptake is dependent on the thyroid area size, we tried to correct UR in order to eliminate the influence of the thyroid area size. In the current study, the standardized size was determined based on the average thyroid area size of the control group and standardized thyroid area size of all individuals.

Our results showed that the linear goodness-of-fit of CUR to TcTU was better than that of UR to TcTU, and the concordance rate between CUR and TcTU was significantly higher than that between UR and TcTU in the small and large thyroid areas. Therefore, the use of CUR as an evaluation parameter may obviously improve the accuracy of semiquantitative ratio in an abnormal thyroid area size.

Furthermore, the results of a better linear relationship (R=0.983) and a higher concordance rate (96.7%) between CUR and TcTU showed that the accuracy of CUR was very similar to that of TcTU. Accordingly, CUR is a more accurate parameter in evaluating $^{99m}$TcO$_4$- thyroid uptake than UR. In a thyroid area of normal size, CUR and UR showed no significant difference in terms of concordance rates with TcTU. This indicates that UR is as highly accurate as CUR under this condition. Therefore, it is not necessary to correct UR under this condition. However, even though UR is corrected as CUR, its accuracy could not be decreased.

The CUR is a simplified semiquantitative parameter as UR. In the CUR formulae, $S_A$, denoting the mean thyroid area size of the control group, is a constant. The $C_a$ and $S_a$ of thyroid ROI, and $C_b$ and $S_b$ of the background ROI are unknown. As long as thyroid ROI and background ROI are outlined, the four unknown parameters are available. Then, CUR can be calculated according to the formulae. The calculation of CUR is simpler than the measurement of TcTU because it does not involve the measurement of the radioactivity of pre- and post-syringes by a dose calibrator, and the imaging of the pre- and post-syringes are performed by a gamma camera.

Therefore, the use of CUR for evaluating thyroid uptake simplifies the operating process, decreases the workload of staff, and shortens the duration of working under gamma ray, thereby reducing the staff’s exposure to radiation in comparison to the measurement of TcTU.

**Clinical significance of CUR in thyroid diseases**

The CUR resembles TcTU and iodine-131 thyroid uptake rate; accordingly, it is an important value in evaluating thyroid diseases (1-7, 25, 26). Our results identified the consistent elevation of both CUR and thyroid hormones as the important feature of Graves’ hyperthyroidism. These features differ from those of subacute thyroiditis. Subacute thyroiditis is characterized by the elevation of the thyroid hormones and reduction of CUR (i.e., separation phenomenon). These features are similar to the results reported in the literature (2-4, 27).

Graves’ hyperthyroidism could be efficiently discriminated from normal thyroid uptake by CUR or UR. However, the URs of some patients with subacute thyroiditis are normal, and sometimes, the UR of some patients with subacute thyroiditis from normal thyroid uptake. Our results indicated that CUR was more effective than UR in differentiating the low uptake of subacute thyroiditis from the normal thyroid uptake. Therefore, differentiating Graves’ hyperthyroidism and subacute thyroiditis is the most important application of CUR.

Thyroid uptake of Hashimoto’s disease and hypothyroidism presented complex features, their CUR showed different levels, namely reduction, normality, and even elevation. The levels of CUR in these diseases were not always consistent with their thyroid function levels. In this study, the CUR of simple goiter was either normal (55.0%; 22/40) or higher than the normal range (45.0%; 18/40), which shows that the decrease of CUR is not the feature of simple goiter.

For Graves’ hyperthyroidism, both CUR and UR were consistently over the normal range. However, CUR and UR were normal in some patients with simple goiter. Therefore, the features of simple goiter were different from those of Graves’ hyperthyroidism. In the patients with simple goiter whose CUR was above the normal range, the UR of some patients was normal, which also differed from that of Graves’ hyperthyroidism. Under this condition, the combination of CUR with UR is valuable in differentiating simple goiter and Graves’ hyperthyroidism. When both CUR and UR increase, the differentiation between Graves’ hyperthyroidism and simple goiter must depend
on their thyroid hormones.

Our results showed that it is sometimes impossible to accurately determine the $^{99m}$TcO$_4^-$ thyroid uptake of patients with partial thyroidectomy by means of UR. The patients with postoperative recurrent Graves’ hyperthyroidism had higher CUR and UR. In this study, 60.9% (14/23) of the patients with postoperative euthyroid also presented higher UR. As a result, it is difficult to differentiate these patients from those with postoperative recurrence by UR.

However, the CURs of 92.9% (13/14) of the patients with increased UR were normal, and the CURs of only 4.3% (1/23) of the patients were slightly higher than the normal range. Therefore, CUR can accurately measure the $^{99m}$TcO$_4^-$ thyroid uptake of these postoperative patients. Accordingly, CUR is better than UR in differentiating between euthyroid patients and patients with postoperative recurrent Graves’ hyperthyroidism.

Research Limitations

The main limitation of this study was that the control group did not include minors; accordingly, it is not known whether the normal values of CUR and TcTu are applicable to minors (especially infants and young children). All of the selected individuals had at least one display of partial thyroid tissue. The patients without any visible thyroid tissue, such as diffuse subacute thyroiditis and total thyroidectomy, were not included in this study given the impossibility of outlining their thyroid ROI. However, the thyroid uptake level of $^{99m}$TcO$_4^-$ of this group was clear for the diagnostic purpose; therefore, the outlining of thyroid ROI was not necessary.

Thyroid area size was defined as the size of functional thyroid tissue rather than the size of full thyroid area or thyroid volume. Therefore, thyroid area size can be only extracted from $^{99m}$Tc-pertechnetate thyroid imaging rather than from other nonfunctional imaging methods. The influence of thyroid thickness on $^{99m}$TcO$_4^-$ thyroid uptake was already reflected in UR; as a result, the UR correction using thyroid volume was not necessarily better than that using thyroid area size. Furthermore, this procedure is of relatively little value in diagnosing hypothyroidism.

Radioiodine uptake test is generally preferred. Thyroid uptake is only an auxiliary diagnostic parameter. The diagnosis of thyroid disease is more effectively made by combining thyroid uptake and the measurements of serum thyroid hormones and thyroid stimulating hormone (TSH).

Conclusion

The present study involved the comparison of the distribution of UR discordance results and analysis of the discordance type of UR results. As the findings indicated, the discordance results of UR were mainly distributed in small thyroid area, and the discordance types of UR results mainly included the overestimation of $^{99m}$TcO$_4^-$ thyroid uptake in small thyroid areas and its underestimation in large thyroid areas.

After standardizing the thyroid area size of the patients, we compared the difference between CUR and UR. The results revealed that the concordance rate between CUR and TcTu and the linear relationship between CUR and TcTu were better than those between UR and TcTu. In other words, CUR is not only a simplified semiquantitative parameter but also a more accurate parameter in evaluating $^{99m}$TcO$_4^-$ thyroid uptake. Therefore, CUR is a valuable parameter in the clinical process of thyroid diseases.

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Conflicts of interest

The authors declared no conflicts of interest.

References

1. Kasagi K, Hidaka A, Misaki T, Miyamoto S, Takeuchi R, Sakahara H, et al. Scintigraphic findings of the thyroid in euthyroid ophthalmic Graves’ disease. J Nucl Med. 1994; 35(5):811-817.
2. Sekulić V, Rajić M, Vlahović M, Ilić S, Bogićević M, Antić S, et al. Thyroid blood flow and uptake of technetium-99m pertechnetate in Graves’ disease. Hell J Nucl Med. 2006; 9(3):173-176.
3. Kidokoro-Kunii Y, Emoto N, Cho K, Oikawa S. Analysis of the factors associated with Tc-99m pertechnetate uptake in thyrotoxicosis and Graves’ disease. J Nucl Med Sch. 2006; 73(1):10-17.
4. Sahlmann CO, Siefker U, Lehmann K, Harms E, Conrad M, Meller J. Quantitative thyroid scintigraphy for the differentiation of Graves’ disease and hyperthyroid autoimmune thyroiditis. Nuklearmedizin. 2004; 43(4):124-128.
5. Meller J, Wisheu S, Munzel U, Behe M, Gratz S, Becker W. Radioiodine therapy for Plummer’s disease based on the thyroid uptake of technetium-99m pertechnetate. Eur J Nucl Med. 2000; 27(9):1286-1291.
6. Reinhardt MJ, Joe A, von Mallek D, Zimmerlin M, Manka-Waluch A, Palmedo H, et al. Dose selection
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for radioiodine therapy of borderline hyperthyroid patients with multifocal and disseminated autonomy on the basis of \(^{99m}\text{Tc}\)-pertechnetate thyroid uptake. Eur J Nucl Med Mol Imaging. 2002; 29(4):480-485.

7. Reinhardt MJ, Bierrmann K, Wissmeyer M, Juengling FD, Brockmann H, von Mallek D, et al. Dose selection for radioiodine therapy of borderline hyperthyroid patients according to thyroid uptake of \(^{99m}\text{Tc}\)-pertechnetate: applicability to unifocal thyroid autonomy? Eur J Nucl Med Mol Imaging. 2006; 33(5):608-612.

8. Schneider PB. Simple, rapid thyroid function testing with \(^{99m}\text{Tc}\)-pertechnetate thyroid uptake ratio and neck/thigh ratio. AJR Am J Roentgenol. 1979; 132(2):249-253.

9. Selby JB, Buse MG, Gooneratne NS, Moore DO. The Anger camera and the pertechnetate ion in the routine evaluation of thyroid uptake and imaging. Clin Nucl Med. 1979; 4(6):233-237.

10. Gao YJ, Han JH, Xie J, Yan XH, Wang JB, Zhu XM, et al. Clinical application of quantitative \(^{99m}\text{Tc}\)-pertechnetate thyroid imaging (Chinese). Chin J Nucl Med. 2002; 22(4):201-203.

11. Sostre S, Parikh S. A visual index of thyroid function. Clin Nucl Med. 1979; 4(2):59-63.

12. She LQ, Mo YB, Zou DH. Predictive value of the visual index of thyroid uptake (VITU) for hyperthyroidism after \(^{131}\text{I}\) therapy (Chinese). J Chin Clin Med Imaging. 2000; 11(4):241-243.

13. Wallack S, Metcalf M, Skidmore A, Lamb CR. Calculation and usage of the thyroid to background ratio on the pertechnetate thyroid scan. Vet Radiol Ultrasound. 2010; 51(5):554-560.

14. Davies S, Barber D, Crisman M, Tan R, Larson M, Daniel G. Quantitative pertechnetate thyroid scintigraphy and the ultrasonographic appearance of the thyroid gland in clinically normal horses. Vet Radiol Ultrasound. 2010; 51(6):674-680.

15. He GR, Ouyang W, Liu JH, Liu WY. Effects of iodine-containing food on \(^{99m}\text{Tc}\) and \(^{131}\text{I}\) uptake in patients with Graves’ disease (Chinese). J First Mil Med Univ. 2004; 24(11):1292-1294.

16. Zhang YJ, Shao F, Wang JL, Jiang CY, Chu SL. Rapid diagnosis of hyperthyroidism with 30min \(^{99m}\text{Tc}\)-pertechnetate thyroid uptake ratio (Chinese). Nucl Tech. 1994; 17(11):672-676.

17. Baskin HJ, Cobin RH, Duick DS, Gharib H, Gutler RB, Kaplan MM, et al. American association of clinical endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002; 8(6):457-469.

18. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedus L, et al. American association of clinical endocrinologists, American college of endocrinology, and associazione medici endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules - 2016 update. Endocr Pract. 2016; 22(5):622-639.

19. Javadi H, Neshandarasli I, Mogharrabi M, Jalalat S, Nabipour I, Assadi M. The effect of an iodine restricted including no sea foods diet, on technetium-99m thyroid scintigraphy: a neglected issue in nuclear medicine practice. Hell J Nucl Med. 2012; 15(1):40-42.

20. Meller J, Becker W. The continuing importance of thyroid scintigraphy in the era of high-resolution ultrasound. Eur J Nucl Med Mol Imaging. 2002; 29(Suppl 2): S425-438.

21. Prakash R. Prediction of remission in Graves’ disease treated with long-term carbimazole therapy: evaluation of technetium-99m thyroid uptake and TSH concentrations as prognostic indicators. Eur J Nucl Med. 1996; 23(2):118-122.

22. Shigemasa C, Teshima S, Taniguchi S, Ueta Y, Mitani Y, Yoshida A. Pertechnetate thyroid uptake is not always suppressed in patients with subacute thyroiditis. Clin Nucl Med. 1997; 22(2):109-114.

23. Ramos CD, Zantut Wittmann DE, Etchebehere EC, Tambascia MA, Silva CA, Camargo EE. Thyroid uptake and scintigraphy using \(^{99m}\text{Tc}\) pertechnetate: standardization in normal individuals. Sao Paulo Med J. 2002; 120(2):45-48.

24. Zantut-Wittmann DE, Ramos CD, Santos AO, Lima MM, Panzan AD, Facuri FV, et al. High pre-therapy \(^{99m}\text{Tc}\) pertechnetate thyroid uptake, thyroid size and thyrostatic drugs: predictive factors of failure in \(^{131}\text{I}\) iode therapy in Graves’ disease. Nucl Med Commun. 2005; 26(11):957-963.

25. Kusić Z, Becker DV, Saenger EL, Paras P, Gartside P, Wessler T, et al. Comparison of technetium-99m and iodine-123 imaging of thyroid nodules: correlation with pathologic findings. J Nucl Med. 1990; 31(4):393-399.

26. Hou H, Hu S, Fan R, Sun W, Zhang X, Tian M. Prognostic value of \(^{99m}\text{Tc}\)-pertechnetate thyroid scintigraphy in radioiodine therapy in a cohort of Chinese Graves’ disease patients: a pilot clinical study. Biomed Res Int. 2015; 2015:974689.

27. Espinoza PG, Guendelman CL, Quevedo Limón LN, Fernández RJ. A comparison between two imaging techniques for the diagnosis of subacute thyroiditis (de Quervain thyroiditis): brief communication. Clin Nucl Med. 2010; 35(11):862-864.