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Relationship between Whole Body Iodine-131 Effective Half-Life and Estimated Glomerular Filtration Rate for Papillary Thyroid Cancer Patients Undergoing Radioactive Iodine Therapy

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Abstract

Background: The aim of this work was to examine the relationship between the estimated glomerular filtration rate (eGFR) as indicator of renal efficiency potentially related to the ability to release radioactive iodine from the patients bodies and the radioactive iodine whole body effective half-life (WBEHL) defined as the time taken for the administered activity to decay to half of its value for papillary thyroid cancer (PTC) patients undergoing radioactive iodine therapy (RAIT) in a tertiary care medical Centre. **Methods:** This retrospective observational study included seventy nine patients, sixty females and nineteen males. The patients were divided in two subgroups, those who have WBEHL of less than 11 hours (n = 51) and those with more than 11 (n = 28) hrs based on k-means clustering technique. **Results:** Analysis of variance (ANOVA) was used to find out if there is a statistically significant difference between the two subgroups **Conclusion:** There was not a statistically significant difference between the short and the longer WBEHL patients' groups analyzed in this study.

Keywords

GFR, Thyroid Cancer, Radioactive Iodine Therapy, Renal Function

1. Introduction

Many published studies aim at identifying the factors affecting the patient effec-

tive half-life or biological half-life in order to model or predict the length of stay in hospitals; since in many countries patient isolation in hospital ward are mandatory by local radiation protection regulations. For the radiation protection team responsible for monitoring the patient and his discharge from the ward planning and organizing the work is important. Deeper Information about effective half-life and the factors contributing to shorten it are justified and maybe very useful.

Glomerular filtration rate (GFR) is an important indicator of renal functions. Conflicting results have been reported about the reduced kidney function and the effective half-life during radioactive iodine therapy (RAIT) for thyroid cancer patients. The method of patient preparation prior to therapeutic administration of Iodine-131 to thyroid cancer patients has been studied as a factor affecting radioiodine renal clearance and consequently the whole body effective half-life and radiation dose, again confliction result have been reported. It is believed that kidney function has a role in the rapidity of urinary clearance of the radioiodine and hence the effective half-life of the whole body radioactivity released from the papillary thyroid cancer (PTC) patients. Estimated glomerular filtration rate (eGFR) is an important indicator of renal function and radioiodine clearance efficiency from the thyroid cancer patients.

It has been hypothesized that renal deficiency may lead to slower iodine-131 excretion rate from the patients leading to longer isolation time in the ward [1]. Hypothyroidism is associated with reduced GFR and increased creatinine levels; and hyperthyroidism results in increased GFR. Also increase in thyroid stimulating hormone (TSH) will influence creatinine levels; therefore the kidney and the thyroid have several interactions. Renal dysfunction has been associated with larger serum creatinine values. Also serum creatinine has been used in the calculation of the estimated glomerular filtration rate (eGFR), therefore examination of the relationship between creatinine levels and shorter isolation time is kind of rational path to explore.

In a recent study it has been shown that patient using high fluid intake, more than 60 ml/hr, alone would not effectively reduce the patient' radiation dose rate at least not more than a well-hydrated state [2]. Another study showed that patients in the hypothyroid phase of more than four weeks and decreased GFR have a longer whole body effective half-life than others [3]. It has been reported that the blood residence time of I-131 is inversely proportional to the renal clearance [4].

Tanaka *et al.* (2018) have found non-significant correlation between TSH and EGFR in subclinical hypothyroidism group of individuals [5]. On the other hand other published studies have shown a significant correlation between elevated serum TSH and renal dysfunction in hypothyroid patients [6] [7].

The aim of this research was to study the potential relationship between whole body effective half-life (WBEHL) and the eGFR for papillary thyroid cancer patients treated with RAIT post thyroidectomy.

2. Methods

This study included 79 patients treated for papillary thyroid cancer at our institution between the years 2018 and 2020; this is a retrospective study and it was approved by the institution research ethics committee, with no patient consent required since their data are totally anonymous.

2.1. Measurement of I-131 Whole Body Effective Half-Life (WBEHL)

Effective half-life was measured using our in-room remote radiation detection system. The system consist of ionization chamber type of detector calibrate to measure radiation dose rates from photons emitted by the I-131 isotope [8]. The ionization chamber is fixed to the room ceiling, located 1.5 meters above the patient bed and calibrated to display the reading in [μSv/hr]. The detection system has a reading display consisting of a personal computer equipment with the appropriate software custom made by a local company and routinely used worldwide. The personal computer display is located outside of the room to avoid unnecessary radiation exposure to radiation protection staff in the hospital. The radiation detection system logs the measured dose rates from the room every 10 minutes and store the data in a database file. A simple table of two columns having the dose rates and the corresponding time of the measurement is generated by the system. The EHL in [hrs] is determined when the dose rate reaches half of its initial value measured after radioactive iodine activity administration. At the time of discharge a plot of the dose rates as a function of the time is generated and is archived as part of the patient file in the personal computer.

2.2. Estimated Glomerular Filtration Rate (eGFR)

Estimated glomerular filtration rate (eGFR) is used in clinical practice to exam renal function status of patients [9]. The body surface area was calculated using the DuBois formula [10].

$$\text{BSA} = \text{Weight}^{0.425}\ [\text{kg}] * \text{Height}^{0.725}\ [\text{cm}] * 0.007184 \quad (1)$$

The GFR is reported in (ml/min/ 1.73 m^2): normalized to a standard body surface area of 1.73 m^2 by multiplying the calculated GFR by (1.73/BSA).

The chronic kidney disease epidemiology collaboration (CKD-EPI) equations were compared with gold standard GFR measurement method using radioisotope Iodine-125 and was found to be the most accurate to use as estimator of the renal function using creatinine, when compared with Cockcroft-Gault equation that estimates clearance of creatinine and the modification of diet in renal disease (MDRD) equation estimating GFR; they found that patients with higher body weight, body mass index (BMI) and age had lower GFR values [11]. We used the CKD-EPI equation proposed by (Levey *et al.*, 2009), to calculate the eGFR [12]

$$\text{GFR} = 144 * (S_{cr}/0.7)^{-1.209} * (0.993)^{\text{Age}} \quad \text{[for Females]} \quad (2)$$

$$\text{GFR} = 141 * (S_{cr}/0.9)^{-1.209} * (0.993)^{\text{Age}} \quad \text{[for Males]} \quad (3)$$

where S_{cr} is the serum creatinine in [mg/dL] and GFR in [mL/min/1.73m^2], age in [years]. The above equations are the most suitable ones for our patient's population [13].

The institutional research ethics committee approved this retrospective research study, and the requirement to obtain informed consent was waived because individual patient information cannot be retrieved or identified.

3. Results

The patients population included in this study are 79 patients, 60 female and 19 male (see **Table 1**).

We can see for the data distribution in **Figure 1** that there is no effect of the estimated eGFR on the effective half–life ($T_{1/2\ eff}$).

4. Discussion

4.1. Thyroid Disease and Renal Function

In a recent study it was found that patients with advanced renal disease, their effective half-life of I-131 is four times higher than the other patients and their urine excretion is very limited [3]. Patient in longer period of thyroid hormone withdrawal may develop a decrease in radioiodine renal clearance, therefore decreased renal function was observed in hypothyroid patients, and further studies are needed to determine the extent of any potential detrimental effects [14].

Despite the fact that upon admission to the ward patients are advised to drink plenty of fluids in order to accelerate the release of the radioactive iodine from their bodies through urine and hence shorten their length of stay in hospital confinement, there is not enough published research to support this idea so far [15].

It has been reported one case in which they concluded that: consumption of plenty of fluids during hospitalization without proper instructions given to the

Table 1. Patients data (n = 79), mean ± standard deviation [minimum-maximum].

variable	values
Age [years]	44 ± 14 [18 - 80]
Weight [kg]	72 ± 14 [36 - 110]
Height [cm]	160 ± 8 [140 - 183]
BMI [kg/m^2]	27.9± 5.3 [15.0 - 40.4]
Administered Activity (MBq)	3725 ± 1027 [1110 - 3725]
Admission radiation dose rate (μSv/hr) @ 1 meter	166 ± 59 [65 - 382]
release radiation dose rate (μSv/hr) @ 1 meter	21.2 ± 8.7 [5 - 42]
Body retained activity at release (MBq)	486 ± 193 [73 - 904]
Whole body effective half-life (hrs)	10.4 ±5.9 [1.8 - 42.4]
eGFR (ml/min/1.73m^2)	111 ± 34 [49 - 215]

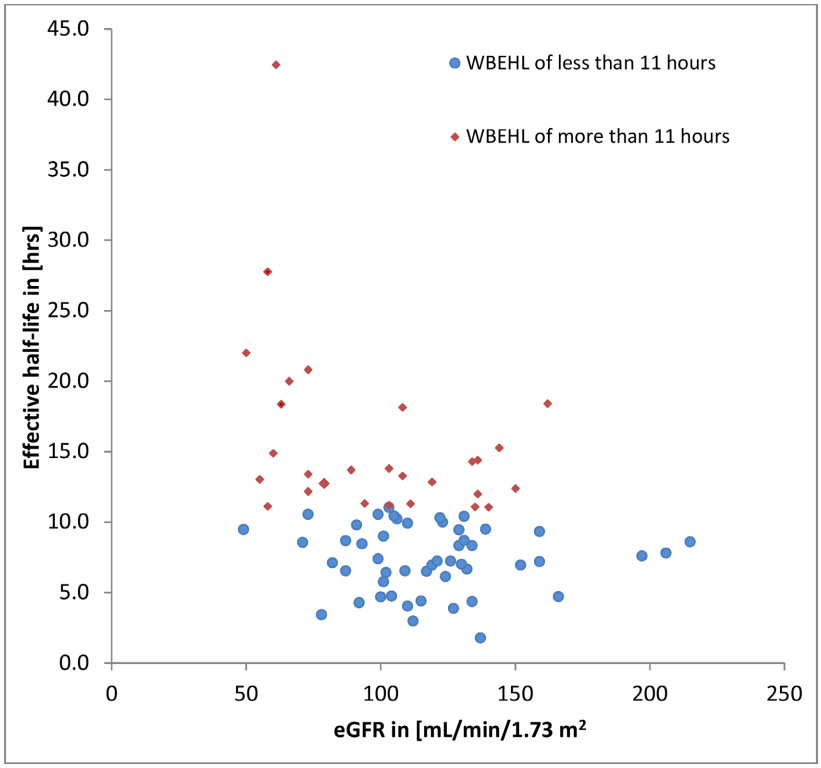

Figure 1. Whole body effective half-life (WBEHL) of Iodine-131 in [hours] as a function of the estimated glomerular filtration rate eGFR in [mL/min/1.73m^2] for the two groups of patients those with WBEHL of less than 11 hours and those with more than 11 hours.

patient may lead to water intoxication resulting from hyponatremia [16]. The law levels of serum sodium inhibits the secretion of antidiuretic hormone (ADH) resulting in an increase of the water excretion by the kidneys resulting in hyponatremia. Bacher et al in their study they found the patients prepared using rhTSH had a shorter effective half-life ($T_{1/2\,Eff}$) that those prepared by THW [3]. They found that duration of hypothyroidism and a GFR value of less than 60 mL/min/1.73m^2 influenced the results.

It has been reported that patients with GFR values of less than 60 ml/min/1.73m^2 have demonstrated clinical and subclinical hypothyroidism indications. We can conclude that a decreased GFR could result in a longer effective half-life for PTC patients [17].

4.2. Patient General Characteristics and Method of Pre-Therapy Preparation

All of patients included in this study had no metastatic lesions outside of the thyroid gland, no metastatic lesions detected in the post ablation scan performed 7 days after RAIT and the all had total thyroidectomy surgeries. All the patients were above eighteen years of age with TSH value > 30 μIU/ml. TSH level of more than 30 mIU/L is recommended for success of ablation treatment [18] [19].

The majority of our patients had L-Thyroxine drug stopped for a minimum time of 3 weeks before the therapeutic iodine administration allowing for the

TSH to reach the value of 30 mIU/L. Few patient had received rhTSH injections before the treatment. In this study we did not study the difference of the mode of preparation since it has been the subject of other published studies [20] [21] [22].

It was previously found that the whole body effective half-life (WBEHL) of Iodine-131 becomes longer in hypothyroid patients with TSH of more than 30 mIU/L as per the applied clinical protocol [15]. Since we apply this protocol in our center, it was found important to study this observation on our patients' population. Thyroid secreting hormones have intrinsic effects on the kidney functions altering the glomerular filtration rate (GFR), electrolyte metabolism and urinary concentration [23].

Ammar *et al.* (2021) have examined the renal function of thyroid cancer patients in Euthyroid and hypothyroid state and found significant difference in urea, creatinine, GFR values between the two groups of patients suggesting a decrease in renal function associated with hypothyroidism [24].

5. Study Limitations

Serum thyroglobulin (TG), Tg-antibody (Tg-Ab), and TSH levels were obtained after withdrawal of L-thyroxine treatment one day before the radioactive iodine administration were not analyzed in this work.

6. Conclusion

Analysis of variance (ANOVA) has been used to find out if there is a statistically significant difference between the two subgroups. Therefore the whole WBEHL cannot be explained merely by the use of eGFR data. The clearance of radioactivity from the patients cannot be explained merely by the GFR and analysis of more variables is warranted.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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