Initial activity-related long-term outcome of iodine-131 treatment for thyroidectomy patients with differentiated thyroid carcinoma

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Abstract

Objective: To determine the outcome of iodine-131 (^{131}I) treatment regimens in thyroidectomy patients with differentiated thyroid cancer. **Materials and Methods:** Based on Taiwan's National Health Insurance Research Database (NHIRD) during the period from January 1, 2000 to December 31, 2010, 390 patients with well-differentiated thyroid cancer who underwent ^{131}I treatment after thyroidectomy were enrolled in this study. Patients were classified into six groups according to the type of thyroidectomy and initial activity regimen of ^{131}I treatment. The clinical outcome of ^{131}I treatment was evaluated by total treatment number and medical expenditure, including costs for hospitalization and laboratory tests together with initial and subsequent ^{131}I treatments. Multiple linear regression analysis was applied to analyze the factor(s) significantly affecting the outcome of ^{131}I treatment. **Results:** Increased activity of the initial ^{131}I regimen reduced the total treatment number significantly for unilateral total thyroidectomy with initial 100-150mCi ^{131}I, and mildly for bilateral total thyroidectomy with initial 100-150mCi ^{131}I and radical thyroidectomy with initial 30-99mCi ^{131}I. Increased activity of the initial ^{131}I regimen reduced total medical expenditure significantly for unilateral, and mildly for bilateral total thyroidectomy both with initial 30-99mCi ^{131}I. **Conclusion:** For patients with specific thyroidectomy for differentiated thyroid cancer, a high initial regimen of ^{131}I treatment is more effective than the low activity regimen. An increased activity of the initial ^{131}I regimen significantly reduced the total treatment number and medical expenditure.

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Introduction

Differentiated thyroid carcinoma (DTC), also known as papillary or follicular thyroid carcinoma, is a slow-growing malignancy that usually presents in adults as an asymptomatic thyroid mass. Iodine-131 (^{131}I) therapy is an established and validated treatment option in patients with well-differentiated thyroid cancer to ablate thyroid remnants after thyroidectomy [1-4]. The administered activity of ^{131}I is usually determined empirically based on clinical and diagnostic imaging [5, 6]. Therefore, evidence-based criteria for ^{131}I treatment regimens should be established based on the types of thyroidectomy.

The National Health Insurance (NHI) program, launched in 1995 in Taiwan, is a mandatory single-payer health care system with nearly 100% coverage rate, including thyroidectomy and ^{131}I treatment. All medical records, including age, sex, and ^{131}I treatment activities, were incorporated into the National Health Insurance Research Database (NHIRD). Based on the NHIRD, this study was conducted to investigate the correlation between the outcome of ^{131}I treatment and its activity regimen after thyroidectomy for thyroid cancer.

Material and Methods

Study population

The study population was included from the Longitudinal Health Insurance Database (LHID) of the NHIRD. Longitudinal Health Insurance Database contains all the original claim data of 1,000,000 beneficiaries enrolled in the year 2010, randomly sampled from the year's registry for beneficiaries of the NHIRD, where registration data of all beneficiaries of

the NHI program during the period from January 1, 2010 to December 31, 2010. Patients with differentiated thyroid cancer undergoing thyroidectomy were selected based on surgery codes between 1997 and 2010. Their medical records of ^{131}I treatments after thyroidectomy were followed up and collected from the initial ^{131}I treatment to December 31, 2010.

Statistical analysis

Descriptive statistics were utilized to analyze the sex, age, and ^{131}I activity distribution among various types of thyroidectomy and initial ^{131}I activities. One-way ANOVA was used to compare the differences in the above distributions among various types of thyroidectomy and initial ^{131}I activities. Multiple linear regression analysis was applied to analyze the factor(s) significantly affecting the outcome of ^{131}I treatment. All statistical analyses were performed using IBM SPSS Statistics 19.0 (IBM Taiwan Corp., Taipei, Taiwan).

Results

Altogether, 390 patients with differentiated thyroid cancer who underwent ^{131}I treatment after thyroidectomy were enrolled in this study. As the activity of ^{131}I treatment is related to the stage of thyroid cancer, the study population was classified into six groups according to the type of thyroidectomy and initial ^{131}I treatment activity, as shown in Table 1. The most frequently performed thyroidectomy was radical thyroidectomy with unilateral neck lymph node dissection. Female patients predominantly accounted for 72.1% to 85.4% and 78.5% on average. The percentage of females was highest in the group with unilateral total thyroidectomy and lowest in the group with bilateral total thyroidectomy, but without significant difference. The average age of initial ^{131}I treatment for every group was between 42.1 and 49.3 years, and 46.1±13.0 in total. The average age of initial ^{131}I treatment was highest in the group with bilateral total thyroidectomy and lowest in the group with unilateral total thyroidectomy, but the difference was not significant.

The average cumulative ^{131}I activity was highest in patients who underwent radical thyroidectomy combined with 100-150mCi initial ^{131}I and lowest in patients who underwent radical thyroidectomy combined with 30-99mCi initial ^{131}I (Table 2). The average number of ^{131}I treatments was higher in the 30-99mCi initial ^{131}I activity, except for radical thyroidectomy. In contrast, the average medical expenditure was higher in the 100-150mCi initial ^{131}I activity for every thyroidectomy.

The outcome of ^{131}I treatment was evaluated by the total treatment number via multiple linear regression analysis, as shown in Table 3. Increased activity of the initial ^{131}I regimen reduced the total treatment number significantly for unilateral total thyroidectomy with initial 100-150mCi ^{131}I, and mildly for bilateral total thyroidectomy with initial 100-150mCi ^{131}I and radical thyroidectomy with initial 30-99mCi ^{131}I. The cumulative activity of ^{131}I also significantly affected the total treatment number for every treatment group; however, age, sex, and follow-up duration were not associated with the total treatment number. Additionally, because the initial activity and cumulative activity of ^{131}I, follow-up duration and cumulative activity of ^{131}I were related in some treatment groups, the interaction terms were modulated to control the interactions.

Table 1. *Demographic characteristics of the study population.*

Type of thyroidectomy and initial ^{131}I activity	Population size	Proportion of females (%)	Average age of initial ^{131}I treatment (years)
Unilateral total thyroidectomy			
30-99mCi	48	85.4	43.1±10.3 (25-63)
100-150mCi	55	81.8	42.1±14.2 (20-82)
Bilateral total thyroidectomy			
30-99mCi	61	72.1	49.3±12.1 (23-71)
100-150mCi	77	76.6	47.0±12.2 (20-75)
Radical thyroidectomy*			
30-99mCi	57	82.5	46.5±14.2 (17-82)
100-150mCi	92	76.1	46.8±13.6 (22-81)
Total	390	78.5	46.1±13.0

**with unilateral neck lymph node dissection*

Table 2. *Characteristics of ^{131}I treatment.*

Type of thyroidectomy and initial ^{131}I activity	Average follow-up duration (years)	Average time interval between thyroidectomy and ^{131}I treatment (years)	Average initial activity of ^{131}I (mCi)	Average cumulative activity of ^{131}I (mCi)	Average ^{131}I treatment number	Average medical expenditure (USD)
Unilateral total thyroidectomy						
30-99mCi	8.5±3.7 (0.2-13.9)	1.3±2.0 (0-7.9)	44±22 (30-99)	98±135 (30-880)	1.9±1.9 (1-10)	1,615±2,563 (304-16,747)
100-150mCi	5.9±4.3 (0.2-13.7)	1.1±2.0 (0-11.3)	113±19 (100-150)	148±72 (100-360)	1.4±0.7 (1-4)	2,350±1,061 (990-5,359)
Bilateral total thyroidectomy						
30-99mCi	4.2±2.6 (0.2-9.2)	1.0±1.8 (0-7.9)	33±12 (30-99)	72±101 (30-590)	1.6±1.5 (1-8)	1,406±1,946 (483-10,821)
100-150mCi	3.5±2.4 (0-9.2)	0.7±1.2 (0-5.4)	112±17 (100-150)	157±130 (100-1020)	1.4±1.0 (1-6)	2,729±1,459 (1,716-9,357)
Radical thyroidectomy						
30-99mCi	3.9±2.5 (0.2-9.3)	0.4±0.8 (0-4.5)	36±15 (30-99)	49±38 (30-210)	1.2±0.5 (1-3)	944±713 (470-3,750)
100-150mCi	3.4±2.4 (0-9.1)	0.8±1.3 (0-7.9)	115±18 (100-150)	174±118 (100-750)	1.6±1.2 (1-8)	3,500±3,414 (1,573-28,619)
Total	4.6±3.4	0.9±1.6	81±42	124±116	1.5±1.2	2,256±2,367

In addition, the outcome of ^{131}I treatment was evaluated by the total medical expenditure via multiple linear regression analysis, as shown in Table 4. Increased activity of the initial ^{131}I regimen reduced total medical expenditure significantly for unilateral, and mildly for bilateral total thyroidec-tomy both with initial 30-99mCi ^{131}I. The cumulative activity of ^{131}I also significantly affected total medical expenditure for most treatment groups except radical thyroidectomy with initial 100-150mCi ^{131}I, and follow-up duration was significantly associated with total medical expenditure for bilateral total thyroidectomy with initial 30-99mCi ^{131}I. The initial activity and cumulative activity of ^{131}I, follow-up duration and cumulative activity of ^{131}I were related in some treatment groups, so the interaction terms were modulated to control the interactions.

Table 3. *Multiple linear regression model for total ^{131}I treatment number.*

Type of thyroidectomy and initial ^{131}I activity	Constant	Sex	Age[1]	Follow-up duration	Initial Activity of ^{131}I	Cumulative activity of ^{131}I	Inter-action[2]	Inter-action[3]	R^2
Unilateral total thyroidectomy									
30-99mCi	0.479	0.418	-0.004	-0.017	0.002	0.033*	0.000*	-	0.91
100-150mCi	0.902*	0.066	0.002	-0.005	-0.008*	0.008*	-	0.000	0.86
Bilateral total thyroidectomy									
30-99mCi	0.580	0.388	-0.006	0.064	0.001	0.020*	0.000*	-	0.72
100-150mCi	1.085*	-0.162	-0.004	0.037	-0.006+	0.007*	-	-	0.83
Radical thyroidectomy									
30-99mCi	1.049*	-0.180	0.000	0.004	-0.011+	0.012*	0.000	-	0.62
100-150mCi	1.136	0.041	-0.005	-0.035	-0.006	0.010*	0.000	0.000	0.77
Total	0.987*	0.079	0.001	-0.020	-0.007*	0.011*	0.000*	0.000*	0.75

*[1]Age of initial ^{131}I treatment, [2]Interaction of initial and cumulative ^{131}I activity, [3]Interaction of follow-up duration and cumulative ^{131}I activity, *P<0.05; +0.05<P<0.1*

Table 4. *Multiple linear regression model for medical expenditure of I ^{131}I treatment.*

Type of thyroidectomy and initial ^{131}I activity	Constant	Sex	Age[1]	Follow-up duration	Initial Activity of ^{131}I	Cumulative activity of ^{131}I	Inter-action[2]	Inter-action[3]	R^2
Unilateral total thyroidectomy									
30-99mCi	995*	-96	-3.3	-61	-12.5*	15*	0.1*	-	0.99
100-150mCi	43	160	-1.0	36	-3.0	22*	-	-1.0*	0.89
Bilateral total thyroidectomy									
30-99mCi	121	42	1.1	36*	-8.6+	16*	0.1*	-	0.98
100-150mCi	262	62	-0.1	-5	0.2	17*	-	-	0.95

(continued)

Radical									
30-99mCi	-60	-101	0.8	16	0.8	19*	-0.0	-	0.95
100-150mCi	-2,491	-326	24.0	219	4.9	21	0.1	-1.8	0.50
Total	-398	-50	7.5	14	-2.1	22*	0.0	-0.6*	0.72

*[1]Age of initial ^{131}I treatment, [2]Interaction of initial and cumulative ^{131}I activity, [3]Interaction of follow-up duration and cumulative ^{131}I activity, *P<0.05; +0.05<P<0.1*

Discussion

The activities of ^{131}I treatment depend on the stages of thyroid cancer, such as 30-99mCi is applied to treat no lymphoid node invasion, along with the types of thyroidectomy. Since the NHIRD does not record the stage of thyroid cancer, we classified them by the types of thyroidectomy and initial ^{131}I activities for unbiased evaluation of the outcomes of the ^{131}I treatment regimen. It should be mentioned that a small patient population with papillary thyroid microcarcinoma (PTMC-not further distinguished from DTC in the database) and/or the use of recombinant human thyrotropin (rhTSH-included in health insurance benefits from 2016), may have been included in our study, yet without affecting the results.

In this study, patients with various thyroidectomy types and ^{131}I regimens had various age, sex, and follow-up duration. Thus, these factors were set into the regression model to control possible confounding factors. Moreover, since the cumulative activity of ^{131}I also affects the number of treatments and medical costs, along with its association with the initial ^{131}I activity, the cumulative activity and interaction terms were considered in the regression model.

Pusuwan et al. (2011) found that a high-dose regimen of radioactive iodine treatment is more effective than the low-dose regimen for hyperthyroidism [7]. Similarly, Fallahi et al. (2012) compared the treatment response of 341 patients with thyroidectomy randomly allocated to the high-dose group (3700MBq) versus the low-dose group (1110MBq), and observed that the higher dose of ^{131}I resulted in successful ablation more often than the low dose [8]. However, in Chinese patients with differentiated thyroid carcinoma, the low dose of 1850MBq radioiodine activity is as effective as a high dose of 3700MBq for thyroid remnant ablation [9]. Similarly, Caglar et al. (2012) compared 800 and 3700MBq ^{131}I for the postoperative ablation of thyroid remnants in patients with low-risk differentiated thyroid cancer, but the success rate was not different [10]. Instead of observing levels of serum thyroglobulin or imaging diagnoses based on above articles, this study, in the context of retrospective research, followed-up the total treatment number and medical expenditure to determine the outcome of ^{131}I treatment regimens in thyroidectomy patients with differentiated thyroid cancer.

In conclusion, for patients with specific thyroidectomy for differentiated thyroid cancer, a high initial regimen of ^{131}I treatment is more effective than the low activity regimen. An increased activity of the initial ^{131}I regimen significantly reduced the total treatment number and medical expenditure.

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