

Health Utility of Patients with Graves' Disease after Two-Year Treatment with Anti-Thyroid Drugs and Radioactive Iodine: a Prospective Study

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Abstract

Introduction: Graves' disease (GD) is the most common cause of hyperthyroidism. Antithyroid hormone drugs (ATD) and radioactive iodine (RAI) are two popular treatments. Choosing treatment methods may lead to different outcomes of treatment.

Objective: The study aimed to evaluate the therapeutic effect between the ATD and the RAI on health utility as an aspect of quality of life (QOL).

Method: A prospective study was conducted. A total of 182 patients with GD were enrolled in the study (151 and 31 patients treated with ATD and RAI, respectively) in Damnoen Saduak Hospital, Thailand, between July 2014 and July 2020. The health utility was measured using the EuroQol (EQ-5D). The comparison of the treatment outcomes between each treatment modality was made using the independent sample t-test.

Result: After two years of the following periods, the patients in the RAI treatment group showed a significant improvement in the QOL than that of the ATD group; in terms of the utility score ($p=0.034$) and remission rate ($p < 0.01$).

Conclusion: RAI demonstrated a better improvement of the health utility than ATD. RAI is suitable for first line treatment strategy for severe GD.

Keywords: Health Utility; Graves' Disease; Anti-Thyroid Drugs; Radioactive Iodine; Quality of Life

Introduction

Graves' disease (GD) is the most common cause of hyperthyroidism which can be found in about 20 to 30 cases per 100,000 population [1]. Thailand, has a prevalence of T3 hyperthyroidism of about 3.5% [2], and the most common occurs at 30 to 60 years. The cause of the disease is the thyroid-stimulating hormone receptor antibody (TRAbs) [1]. Autoimmune disorder is characterized by goiter, hyperthyroidism and, in 25% of patients, Graves ophthalmopathy [3].

The three therapeutic approaches for treating Patients with GD are antithyroid drugs (ATDs), RAI therapy, and surgical thyroidectomy. Higher physician preference for ATD is similar to Europe, Latin America and other Asian countries. Geographic differences exist in the use of ATD, radioactive iodine, and thyroidectomy. All three treatment options are useful, but each treatment approach has advantages

and drawbacks. Patient-centered communication and shared decision making are becoming increasingly important in determining the most suitable treatment option. The treating physician and patients should discuss the logistics, cost of care, expected recovery time, benefits, disadvantages and possible side effects for each treatment option. The severity of thyrotoxicosis may also influence the decision [4]. Choosing a treatment method should include considering the outcome with various aspects including clinical outcome, economic elements and quality of life (QOL) [5]. Generally, the treatment outcome of the QOL aspects is less assessed as compared with the clinical aspects. The two types of QOL measures for health are general and disease-specific measures. The health utility (HU) is a standard general quality of life measure used in health economics assessment because scores can be reported as index values. The HU's benefit is calculating the quality-adjusted life year (QALY), the most common health outcome in cost effectiveness analysis and cost utility [5].

Studies on HU as the aspect of QOL among patients with GD in many countries were frequently conducted using conventional and specific tools [6-8]. Most studies have found that patients had lower rates of HU as the severity of the disease [9,10]. In Thailand, there is only one study of QOL in patients with GD, a cross-sectional study that measured patient QOL over a year using EQ-5D [11]. Moreover, the HU of patients, treated with the ATD and RAI remains unclear. The researcher investigated the therapeutic effects of the two treatments among patients with GD HU after a two year-period of treatment to gain useful information for selecting treatment methods and promoting patients' health care with GD.

Purpose of the study

This paper aimed to compare the HU after treatment for two years and the utility change among patients with GD receiving ATD and RAI treatment.

Materials and Methods

The study employed a two-year prospective design where HU data were collected from all patients with GD treated with ATD and RAI using the EQ-5D utility assessment form, established in Damnoen Saduak Hospital, and general hospitals in central Thailand, from July 2014 to July 2020. A total of 182 patients with GD were enrolled in the study (151 and 31 patients treated with ATD and RAI, respectively). HU was measured using a standard questionnaire of EQ-5D-3L, which was translated to Thai. The EQ-5D-3L descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels: no problems, some problems and extreme problems. The patients were asked to indicate their health state by ticking the box next to the most appropriate statement in each of the five dimensions. The intra-class correlation coefficients (ICCs) = 0.74 to 0.86 test for structural validity had a Spearman's correlation coefficient between 0.48 and 0.60 ($p < 0.01$) [12,13]. Patients' clinical and laboratory characteristics were included in the study.

Data were analyzed using the Statistical Package for Social Science, Version 21. Descriptive statistics of frequency, percentage, mean and standard deviation were performed for categorical and continuous variables, respectively. The independent sample t-test was applied to investigate the differences between means. The chi-square test was used to determine statistically significant differences between the different categorical variables. QOL was assessed using Pearson's correlation coefficient.

Ethical considerations

The study was approved by the Clinical Research Ethics Committee of the participating hospitals (No.6/2558). The researcher participated voluntarily in the interviews. First, the purpose of the study was explained to them verbally and in writing, then the informed consent process was carried out. According to the applicable data protection, alphanumeric codes were used to guarantee the confidentiality of the information provided and the participants' anonymity.

Results and Discussion

Results

Clinical and laboratory characteristics of the patients

Most patients were female (73.08%) and treated with an antithyroid hormone (82.97%). During diagnosis, the majority were aged 41 to 50 years (24.18%) followed by 31 to 40 years (21.98%). In all, 62.09% of patients had no underlying disease. As for patients with an underlying condition, hypertension (20.33%) was the most common, followed by hyperlipidemia (15.38%), as shown in table 1.

Variable	Mode of treatment (N=182)				p-value
	Total		ATD	RAI	
	N	(%)	N	N	
Age (Years) M ± SD: 24.9 ± 6.21 (range: 17 - 40)					0.123
Less than 20	6	3.3	5	1	
21-30	28	15.38	22	6	
31-40	40	21.98	32	8	
41-50	44	24.18	37	7	
51-60	39	21.42	32	7	
Above 60	25	13.74	23	2	
Sex					0.053
Male	49	26.92	45	4	
Female	133	73.08	106	27	
Underlying condition					0.476
No	113	62.09	92	21	
Yes	69	37.91	59	10	
Hypertension	37	20.33	23	14	
Dyslipidemia	28	15.38	20	8	
Diabetes	13	7.14	10	3	

Table 1: Demographic Characteristics of GD Patients.

The most common symptoms were weight loss (95.60%), followed by palpitations (82.42%). The most common signs were tachycardia (69.78%), followed by tremor (57.14%), as shown in table 2. The average time since symptoms were diagnosed was 3.37 months, as shown in table 3.

Symptom	N	%	Signs	N	%
Weight loss	174	95.60	Tachycardia	127	69.78
Palpitations	150	82.42	Tremor	104	57.14
Increased appetite	99	54.40	Warm moist palms	87	47.80
Hyperdefecation	98	53.85	Diffuse palpable goiter	78	42.86
Tremulousness	48	26.37	Atrial fibrillation	19	10.40
Dyspnea	33	18.13	Periorbital edema	8	4.40
Eye symptoms	8	4.40	Muscle weakness	3	1.65
Nervousness (anxiety)	7	3.85	Pretibial myxedema	2	1.10

Table 2: Signs and Symptoms of Patients with GD.

Variable	Total	ATD (N=151)	RAI (N=31)	p-value
	M ± SD	M ± SD	M ± SD	
Duration of symptoms (month)	3.37 ± 3.70	3.30 ± 3.58	3.71 ± 4.307	0.574 ^a
Heart rate (beat/minutes)	107.48 ± 23.66	107.38 ± 24.05	107.97 ± 22.03	0.901 ^a
FT3 level (pg/mL)	13.58 ± 6.16	13.20 ± 5.94	15.42 ± 6.92	0.067 ^a
TSH level (μIU/mL)	0.02 ± 0.07	0.02 ± 0.06	0.03 ± 0.10	0.358 ^a
Anti-TPO (IU/mL)	160.84 ± 195.35	171.52 ± 200.13	108.85 ± 163.13	0.104 ^a
Anti-TG (IU/mL)	334.14 ± 719.10	309.13 ± 645.26	455.96 ± 999.751	0.302 ^a
TRAbs (IU/L)	5.91 ± 9.31	5.62 ± 8.86	7.34 ± 11.35	0.349 ^a
Remission: N (%)	98 (53.80)	70 (46.36)	28 (90.32)	<0.01 ^b

Table 3: Clinical and laboratory characteristics of the patients.

^a Independent sample t-test, ^b Chi-square test.

The first diagnostic laboratory results found that the mean FT3 level was 13.58 ± 6.16 pg/mL. The mean TSH level was 0.23 ± 0.07 μIU/mL, the Anti-TPO level was 160.84 ± 195.35 IU/mL, the Anti-TG level was 334.14 ± 719.10 IU/mL and the TRAbs level was 5.91 ± 9.31 IU/L, as shown in table 4. After two years of treatment, the group of patients treated with RAI had significantly more recoveries than those who took ATD (p < 0.01): 90.32% (28 patients) vs. 46.36% (70 patients) respectively, as shown in table 3.

EQ-5D Item (N=182)	Before treatment	2-year posttreatment
	N (%)	N (%)
1. MOBILITY		
- I have no problems in walking about	27 (14.83)	107 (58.79)
- I have some problems in walking about	153 (84.07)	75 (41.21)
- I am confined to bed	2 (1.10)	0
2. SELF-CARE		
- I have no problems with self-care	34 (18.68)	140 (76.92)
- I have some problems washing or dressing myself	143 (78.57)	42 (23.08)
- I am unable to wash or dress myself	5 (2.75)	0
3. USUAL ACTIVITIES, e.g., work, study, housework		
- I have no problems performing my usual activities	15 (8.24)	145 (79.67)
- I have some problems performing my usual activities	162 (89.01)	37 (20.33)
- I am unable to perform my usual activities	5 (2.75)	0
4. PAIN/DISCOMFORT		
- I have no pain or discomfort	20 (10.99)	124 (68.13)
- I have moderate pain or discomfort	114 (62.64)	52 (28.57)
- I have extreme pain or discomfort	48 (26.37)	6 (3.30)
5. ANXIETY/DEPRESSION		
- I am not anxious or depressed	78 (42.86)	159 (87.36)
- I am moderately anxious or depressed	91 (50.00)	23 (12.64)
- I am extremely anxious or depressed	13 (7.14)	0

Table 4: Distribution of the participants according to their responses to health dimension in EQ-5.

Health utility

When considering each dimension of the EQ-5D utility model before treatment, most of the subjects had moderate problems. The severe problem dimensions included pain/discomfort, 48 (26.37%), followed by anxiety/depression, 13 (7.14%). The most affected areas were performing daily activities, 162 (89.01%). Moreover, regarding ability to move, 153 walking problems were reported (84.07%), as shown in table 4.

After treatment for two years, most patients had no problems in each dimension. Concerning mobility, 41.21% of patients reported gait problems followed by pain/discomfort dimension with moderate pain or discomfort, -28.57%, as shown in table 4.

The mean pretreatment utility was 0.234 ± 0.290 (-0.454 to 0.766). The mean two-year posttreatment utility was 0.937 ± 0.149 (0.095 to 1.000) at completion of the treatment. The mean utility changes were 0.704 ± 0.289 (0.030 to 1.450), as shown in table 5.

Health utility	Treatment modality		p-value
	ATD	RAI	
Before treatment	0.249 ± 0.296 (-0.454 - 0.766)	0.160 ± 0.249 (-0.454 - 0.546)	0.039
2-year posttreatment	0.932 ± 0.153 (0.095 - 1.000)	0.964 ± 0.121 (0.425 - 1.000)	0.211
Utility value change	0.683 ± 0.295 (0.030 - 1.450)	0.804 ± 0.242 (0.450 - 1.450)	0.034

Table 5: Health utility between ATD and RAI using the Independent samples t-test.

Before treatment, the mean antithyroid hormone class utility was 0.249 ± 0.296 (-0.454 to 0.766), and the mean of RAI group utility was 0.160 ± 0.249 (-0.454 to 0.546). The RAI was significantly lower than the antithyroid hormone group ($p = 0.039$), as shown in table 5.

After two years of treatment, the mean ATD group utility was 0.932 ± 0.153 (0.095 to 1.000). The mean utility of the RAI group was 0.964 ± 0.121 (0.425 to 1.000), as shown in Table 5. Mean utility values changed from before treatment to complete treatment for RAI (mean utility change was 0.804 ± 0.242) and was significantly higher than that of ATD treatment (mean utility change 0.683 ± 0.295) ($p = 0.034$).

Discussion

The remissions at two years of treatment were significantly greater than those in the RAI treatment group ($p < 0.01$). Similarly, another study indicated antithyroid hormone use had a remission rate of approximately 40 to 50% [14,15]. Among patients treated with RAI, 90.32% of the patients were cured, similar to the study conducted by Ross DS., Braga M, Alexander EK, Ma C, Xie J., *et al.* reporting remission rates more than 80 to 95% [16-19].

When considering each dimension of the pretreatment EQ-5D utility model, most patients reported moderate problems, which was consistent with the study of Valeerat Vongkasem., *et al.* [11]. The dimensions that revealed severe problems were pain/discomfort with "extreme pain or discomfort" as much as 26.37%, followed by "extremely anxious or depressed" 7.14%. The areas that exhibited the most significant impact were "problems with performing my usual activities" and "problems in walking about," respectively. Unlike Valeerat Vongkasem., *et al.*'s study the results showed mobility problems involved walking, maybe due to the cross-sectional study design where some of patients had already been treated [11]. After two years of the utility data, considering each dimension of the EQ-5D utility model, most patients did not have any problems. The areas that had severe problems involved "mobility". The patients indicated some walking problems about, 41.21%, followed by 28.57% reporting moderate pain or discomfort concerning the pain/discomfort dimension with no other studies to compare.

Both modalities showed a statistically significant increase in mean utility after two years' treatment. It showed that both treatments improved the patient's QOL. When comparing utility before giving treatment, the utility of RAI treatment (mean HU = 0.160 ± 0.249) was significantly lower than ATD therapy (mean HU = 0.249 ± 0.296) ($p = 0.039$). This indicated that the groups of patients treated with RAI experienced worse QOL at diagnosis that may reflect severe symptoms.

When considering the average utility value change from before to complete treatment, that of the RAI group was higher than that of the ATD therapy ($p = 0.034$) indicating that patients treated with RAI revealed that QOL changed for the better.

Conclusion

The HU before RAI treatment was significantly lower than that of the ATD therapy group, indicating that the group of patients receiving RAI experienced worse symptoms. Further, the changed average utility was significantly higher than that of the ATD therapy group. RAI demonstrated a better improvement of HU than that of the ATD group. Therefore, RAI was suitable for first line treatment strategy regarding severe GD.

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