Cost-Effectiveness Analysis of Antithyroid Drug Therapy, 
\(^{131}\)I Therapy and Subtotal Thyroidectomy for Graves’ Disease

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The objective of this study was to assess the cost-effectiveness of antithyroid drug (ATD) therapy vs. radioiodine therapy (RIT) vs. subtotal thyroidectomy (STT) by calculating expected lifelong cost and utility based on Graves’ disease patients’ responses to questionnaires using a decision-tree sensitivity analysis and relevant variables. The decision-tree sensitivity analysis to determine expected lifelong cost and utility in Graves’ disease patients was designed on the basis of the 4 competing strategies consisting of: (1) ATD therapy plus RIT strategy, (2) ATD therapy plus STT strategy, (3) low-fixed-dose (185 MBq) RIT alone strategy, and (4) high-fixed-dose (370 MBq) RIT alone strategy. One-way sensitivity analysis was designed in the ATD therapy plus RIT strategy, for replacement with RIT in place of ATD, ranging from a 100% incidence of ATD side effects to 30%. The low-fixed-dose RIT alone strategy was least costly, and the high-fixed-dose RIT alone strategy most costly. The lifelong utility of high-fixed-dose RIT alone strategy with a 5% rate of discounting was highest (lifelong utility for 30 years : 15.2/patient), and the utility of the ATD plus RIT strategy with 1% side effects of the ATD was lowest (14.1/patient). The cost-effectiveness ratio was lowest (¥5 008/utility) in a low-fixed-dose RIT alone strategy. In conclusion, a low-fixed-dose RIT alone strategy is preferred treatments in view of cost-effectiveness ratio, and RIT should be used more widely in Japan.

Key Words : \(^{131}\)I therapy, Graves’ disease, cost-effectiveness analysis, antithyroid drug, thyroidectomy

1. Introduction

Graves’ disease is common, and there are multiple treatment options, such as antithyroid drug (ATD) therapy, radioiodine (\(^{131}\)I) therapy (RIT), and subtotal thyroidectomy (STT: bilateral STT, or total lobectomy, isthmusectomy, and subtotal lobectomy on the other side). No single treatment alone usually results in permanent euthyroidism, because none of them is a treatment for the Graves’ disease itself. Treatment options vary from country to country, although RIT has been established as a treatment for Graves’ disease without serious complications for over 50 years\(^{1, 2}\). ATD therapy is favored as the first-line therapy in European countries and Japan, whereas most Graves’ disease patients in the United States (US) are treated by RIT\(^{3, 4}\).

ATD (thiamazole) therapy has been used worldwide, but it is associated with a variety of side effects, as well as one well-known adverse effect, i.e., potentially life-threatening agranulocytosis\(^{5, 6}\). Antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis has also recently been reported as an adverse effect of ATD, especially in Japan\(^{7}\). Despite long-term, daily ATD therapy, usually for 18 months or more,
the highest remission rate reported has been approximately 50%\cite{6, 6}. There is some concern about the potential for side effects of each treatment\cite{5}. A major side effect of RIT is an impairment of Graves’ ophthalmopathy\cite{3}. RIT shows promise of becoming the treatment of choice for Graves’ disease, because of high remission rate and lower frequency of side effects. Several studies have attempted to identify the optimal therapy for Graves’ disease\cite{8, 9, 10, 11, 12}. However, no detailed cost-effectiveness analyses of ATD therapy versus RIT versus STT for Graves’ disease by means of decision-tree sensitivity analysis, which is a useful tool for resolving uncertainty in decision making, have ever been published. Surgery is seldom used to treat hyperthyroidism anywhere in the world\cite{13, 14}, but STT remains a popular and promising treatment in Japan, because STT reliably results in a euthyroid state in a shorter period, and many skilled surgical teams in Japan have had a great deal of experiences. The cost of treatment is likely to become an increasingly important consideration in the near future. However, there has been no evidence that RIT is superior to ATD therapy as a treatment for Graves’ disease from a cost-effectiveness standpoint.

Health economics has emerged as an important discipline in Japan over the last few decades, the same as in the US and Europe. Increasing interest in health economics has been driven both by the advent of the aged societies and by the perceived need to control rising health-care costs. Cost-benefit analysis with regard to health-care costs has been becoming an important policy for dealing with both uncertainty and complex value judgments. Since Graves’ disease is a common clinical entity, it is very important to assess quality of life (QOL) during the lifetime of each patient as well as medical economics.

The objective of this study was to assess the cost-effectiveness of ATD therapy versus RIT versus STT by calculating expected lifelong medical costs and utility based on the responses of Graves’ disease patients to questionnaires. We developed our published data\cite{12} and performed a decision-tree sensitivity analysis using the relevant variables to determine the expected cost and utility of treating Graves’ disease patients. The present study built upon and expanded the analysis performed in our previously published paper on the cost-effectiveness of Graves’ disease\cite{10}.

2. Materials and Methods

2·1 Four competing strategies

The preference of the patient is paramount in the decision process. To determine the expected lifelong cost and utility of treatment of Graves’ disease patients, the decision-tree sensitivity analysis was designed on the basis of the 4 competing treatment: (1) an ATD plus RIT strategy, (2) an ATD plus STT strategy, (3) a low-fixed-dose RIT alone strategy (185 MBq), (4) a high-fixed-dose RIT alone strategy (370 MBq).

ATD therapy is generally used in one of two ways: as the primary treatment for Graves’ disease and as preparatory therapy before RIT or STT or total thyroidectomy. In the first two strategies, we assumed that an ATD was used as the initial primary treatment for Graves’ disease. Only patients who had side effects of ATD underwent RIT in the ATD therapy plus RIT strategy or STT in the ATD therapy plus STT strategy. In patients presenting with side effects after ATD therapy, there is no criterion which option to choose, RIT or STT. The study
is a presumptive, assumed and prospective cohort analysis. Patients in whom no remission had been achieved after ATD therapy for two years continued to take ATD daily for 30 years in the ATD plus RIT strategy and the ATD plus STT strategy. Thus, in the first two strategies, ATD is given to the patients as a final therapeutic decision, except in those in whom remission is achieved and in those who develop side effects.

2.2 Decision trees

A decision-tree analysis was designed to determine the expected cost and utility. The details of the decision-tree sensitivity analysis have been described elsewhere\(^{15,16}\). Decision-tree is generally constructed of choices and potential outcomes of the choices. All conditional probabilities of each outcome in the tree are calculated and obtained as a function of the variables by Bayesian analysis, that is,

\[
P(+|\text{test}) = \frac{P \times S + (1-P) \times (1-S)}{P \times S + (1-P) \times (1-S) + P \times (1-S) + (1-P) \times S}
\]

where \(P\) = prevalence, \(S\) = sensitivity, \(Sp\) = specificity.

In the current study we designed a non-pregnant female patient model in which the onset of Graves’ disease was assumed to have occurred with little or no exophthalmos with less than Class 2 (soft tissue involvement and proptosis < 22 mm) at the age of 40 and in which the first complaint of thyrotoxic symptoms and moderate goiter (thyroid weight: 40 g) had been made 2–3 months previously. The patient was assumed to weigh > 50 kg and to have serum free thyroxin (free \(T_4\)) level of 5 ng/dL or more. A simulation of 1 000 patients was set up, and each patient was assumed to undergo a 30-year-long cohort study of each strategy in which a decision-tree and baselines values of relevant variables were used.

The ATD plus RIT strategy is shown on Fig. 1. The assumptions were as follows: patients were given 1-methyl-2-mercaptopimidazole (methimazole) 30 mg daily for 3 months and with a daily dose of 10 mg for 21 months thereafter. ATD therapy was discontinued in the patient group that experienced a remission (euthyroidism), but continued at 10 mg daily for 28 years in the uncontrolled group that did not experience a remission. On the other hand, the patient group that experienced side effects of
ATD underwent RIT at a dose of 185 MBq one to three times at intervals of 6 months until remission was achieved. If permanent hypothyroidism developed after RIT, \( l \)-thyroxin was replaced at a daily dose of 100 \( \mu g \).

The ATD plus STT strategy is shown in Fig. 2. The assumptions were: patients were given methimazole 30 mg daily for 3 months and 10 mg daily for 21 months thereafter. ATD therapy was discontinued in the patient group that experienced remission, but the uncontrolled patient group that did not experience a remission underwent STT. The patient group that developed side effects of ATD was also treated by STT. The incidence of side effects of ATD was assumed to be 10% in the ATD therapy plus STT strategy. When permanent hypothyroidism develops in patients who have undergone STT, \( l \)-thyroxin was replaced at a daily dose of 100 \( \mu g \). Mortality and complications following STT were assumed to be zero.

The incidence of agranulocytosis due to ATD was also assumed to be 0.5%. An agranulocytosis patient was assumed to be hospitalized for 4 weeks, and the cost was calculated based on the Disease Procedure Combination (DPC) payment system.

The low-fixed-dose RIT alone strategy is shown in Fig. 3. The assumptions were: all patients were first given a low-fixed dose of radioiodine \((^{131}I, 185 \text{ MBq})\). The absorbed dose was approximately 70 Gy to the thyroid gland. The patient group that was not controlled with RIT underwent repeated RIT. When permanent hypothyroidism developed, \( l \)-thyroxin was replaced at a daily dose of 100 \( \mu g \). In the high-fixed-dose RIT alone strategy group the assumptions were: all patients were first given a high fixed dose of radioiodine \((^{131}I, 370 \text{ MBq})\). The absorbed dose was approximately 140 Gy to the thyroid gland. When hypothyroidism eventually developed, \( l \)-thyroxin was replaced at a daily dose of 100 \( \mu g \) in all patients.
2.3 One-way sensitivity analysis

The side effects of ATD are variable, and their frequency is as high as 30%, when mild side effects are included. The choice of therapy for Graves' disease depends on the patient's preference. Therefore, one-way sensitivity analysis was designed for replacement of ATD therapy with RIT, ranging from 1% to 30%, in the ATD plus RIT strategy.

2.4 Variables, cost, utility

The baseline values of the relevant variables used in the decision trees are shown in Table 1. Remission rates in response to ATD therapy and RIT were assumed to be 40% and 74%\(^{17}\), respectively. The relapse rates after low-fixed-dose RIT and STT are cited from the literature\(^{17,18}\). Annual or decade incidences of hypothyroidism after low-fixed-dose RIT are also shown in Table 1\(^{19,20}\). The relapse rate and incidence of hypothyroidism after high-fixed-dose RIT were assumed to be 0% and 100%, respectively.

Present value is calculated as $PV = C / (1 + r)^t$, where $PV$ is the present value, $C$ is the amount of money paid, $r$ is the risk-adjusted discount rate, and $t$ is the period after which future money is to be paid. Future costs in our series were discounted 5%. Utility was also discounted 5%.

The costs refer to billed costs based on the Japanese national insurance reimbursement system. The expected costs of the competing strategies were calculated by summing the products of the probabilities and values of the outcome of each strategy. Overhead costs (direct non-medical costs, productivity costs), regulatory costs, and maintenance costs were not allocated in the present study. The cost was calculated in US dollars at a yen-dollar conversion rate of ¥110 to $1.

We used a rating scale method, the feeling thermometer, to determine short-term and lifelong utility. The short-term utility was calculated on the basis of QOL according to the 45 completed questionnaires returned by the 50 female patients (20 to 61-year-old women; mean age: 36 years) to questionnaires. Short-term utility can be determined on the basis of the present QOL of the Graves' disease patient, because the patient might experience several different types of thyroid states, i.e., hyperthyroid state, euthyroid state after ATD therapy or RIT, euthyroid state with hormone replace-
Table 1  Baseline values of relevant variables used in the decision trees

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Remission rate</strong></td>
<td></td>
</tr>
<tr>
<td>ATD medication</td>
<td>40%</td>
</tr>
<tr>
<td>RIT Low-fixed-dose (185MBq)</td>
<td>74%</td>
</tr>
<tr>
<td>STT</td>
<td>80%</td>
</tr>
<tr>
<td><strong>Relapse rate</strong></td>
<td></td>
</tr>
<tr>
<td>RIT</td>
<td></td>
</tr>
<tr>
<td>Low-fixed-dose (185MBq)</td>
<td>26%</td>
</tr>
<tr>
<td>High-fixed-dose (370MBq)</td>
<td>0%</td>
</tr>
<tr>
<td>STT</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Hypothyroidism Incidence</strong></td>
<td></td>
</tr>
<tr>
<td>Low-fixed-dose RIT</td>
<td></td>
</tr>
<tr>
<td>one year</td>
<td>11%</td>
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<tr>
<td>ten years</td>
<td>30%</td>
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<tr>
<td>twenty years</td>
<td>40%</td>
</tr>
<tr>
<td>thirty years</td>
<td>50%</td>
</tr>
<tr>
<td>High-fixed-dose (370MBq)</td>
<td>100%</td>
</tr>
<tr>
<td>STT</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
</tr>
<tr>
<td>ATD (thiamazole; 5mg MMI)</td>
<td>¥10/tablet</td>
</tr>
<tr>
<td>L-thyroxin (50µg)</td>
<td>¥10/tablet</td>
</tr>
<tr>
<td>RIT</td>
<td></td>
</tr>
<tr>
<td>Low-fixed-dose (185MBq)</td>
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<td>High-fixed-dose (370MBq)</td>
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<td><strong>Utility</strong></td>
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<td>Remission after ATD medication</td>
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<tr>
<td>No remission with ATD medication</td>
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<tr>
<td>Remission after RIT</td>
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<td>Hypothyroidism after RIT</td>
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<tr>
<td>Remission after STT</td>
<td>0.95</td>
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<tr>
<td>Hypothyroidism after STT</td>
<td>0.92</td>
</tr>
<tr>
<td>Agranulocytosis with sepsis</td>
<td>0.20</td>
</tr>
</tbody>
</table>
ment therapy. The 45 patients were diagnosed as Graves' disease 2 to 15 years previously. Maximum (best fitness and health) and minimum (death) utility were scored 1.0 and 0.0, respectively. The 45 patients had no or little Graves' ophthalmopathy (≤Class 2) at the onset. The 41 questionnaire responders had undergone both ATD therapy and RIT, and the four both ATD medication and STT. All patients had the detailed explanation of QOL, which comprises four components: somatic sensation (symptoms such as palpitations, sweating, fatigue), physical function (daily activity), psychological state, and social interaction. The rating scales were obtained in the following state: 1) euthyroid state on ATD therapy, but with no remission yet, 2) euthyroid state after completion of ATD therapy, 3) euthyroid state after RIT, 4) hypothyroid state on replacement therapy after RIT, 5) euthyroid state after STT, 6) hypothyroid state on replacement therapy after STT. The patients who had undergone STT had no major complications, such as dysphonia, hoarseness, or hypoparathyroidism. Two patients experienced agranulocytosis with sepsis after the administration of ATD therapy.

3. Results

The lifelong (30 years) medical cost for 30 years with a 5% rate of discounting was ¥84 715 (US$770) per patient for the ATD plus RIT strategy with a 1% incidence of side effects of ATD, ¥82 085 (US$746) for a 10% incidence, ¥78 391 (US$713) for a 20% incidence, ¥82 035 (US$746) for a 30% incidence, ¥91 995 (US$836) for the ATD plus STT strategy, ¥74 614 (US$678) for the low-fixed-dose RIT alone strategy, ¥154 459 (US$1 404) for the high-fixed-dose RIT alone strategy. Thus, the cost of the low-fixed-dose RIT alone strategy was lowest, and the cost of the high-fixed-dose RIT alone strategy was the highest (Fig. 4).

The results for the utility of the strategies were: 1) euthyroid state on ATD therapy, but with no remission yet: 0.86 ± 0.12 (n = 41), 2) euthyroid state after completion of ATD therapy: 0.99 ± 0.01 (n = 20), 3) euthyroid state after RIT: 0.98 ± 0.02 (n = 41), 4) hypothyroid state on replacement therapy after RIT: 0.93 ± 0.05 (n = 17), 5) euthyroid state after STT: 0.95 ± 0.02 (n = 4), 6) hypothyroid state on replacement therapy after STT: 0.92 ± 0.03 (n = 4), 7) no remission state: 0.65 ± 0.12 (n = 41), 8) agranulocytosis with sepsis: 0.2 ± 0.00 (n = 2).

The lifelong utility (the sum of utility values) for 30 years with a 5% rate of discounting was 14.1 per patient for the ATD plus RIT strategy with a 1% incidence of side effects of ATD (cost-effectiveness ratio: ¥6 008/utility), 14.2 for a 10% incidence (cost-effectiveness ratio: ¥5 781/utility), 15.0 for a 20% incidence (cost-effectiveness ratio: ¥5 226/utility), 15.0 for a 30% incidence (cost-effectiveness ratio: ¥5 469/utility), 14.9 for the ATD plus STT
strategy (cost-effectiveness ratio: ¥6 174/utility), 14.9 for the low-fixed-dose RIT alone strategy (cost-effectiveness ratio: ¥5 008/utility), 15.2 for the high-fixed-dose RIT alone strategy (cost-effectiveness ratio: ¥10 162/utility). Thus, the lifelong utility of the high-fixed-dose RIT alone strategy was highest, and the lifelong utility of the ATD plus RIT strategy with a 1% side effects of ATD was lowest (Fig. 5).

4. Discussion

4.1 Strategy results

Graves’ disease is a common clinical form of thyroid disease, and its annual incidence is approximately 1%\(^{21}\). The treatment of Graves’ disease is still a matter of controversy. In the US, RIT is the preferred treatment for Graves’ disease in adult patients, whereas in European countries and Japan ATD therapy is recommended and conducted more frequently than RIT. RIT accounts for 70% of all treatment of Graves’ disease in the US, 22% in the European countries, and 11% in Japan\(^{22}-^{24}\). The lower rate in Japan is likely to be due to reluctance or unwillingness to use radiation because of the atomic bomb casualties in Hiroshima and Nagasaki in World War II.

Some investigators have stated that RIT is more cost-effective for Graves’ disease than the ATD therapy in the US and European countries\(^{8}-^{11}\). However, medical costs and the insurance reimbursement system in Japan differ greatly from the costs and insurance systems in the US and European countries. Few investigators have reported whether RIT is superior to ATD therapy or STT for Graves’ disease from a cost-effectiveness viewpoint\(^{12}\).

We used a 40-year-old non-pregnant female as a model of the current study, unlike our previous study using a non-pregnant female model in which the onset of Graves’ disease was at the age of 30\(^{12}\). The reasons for it are that a 30-year-old female may deliver a baby in several years later, and that it is likely that she or a physician will prefer ATD treatment rather than RIT. In our series the low-fixed-dose RIT alone strategy with \(^{131}\)I resulted in the lowest lifelong (30 years) cost, ¥74 614 (US$678) per patient, and the relatively high lifelong utility, 14.9 per patient (cost-effectiveness ratio : ¥5 008/utility). These results indicate that the low-fixed-dose RIT alone strategy is superior to other treatment options from a cost standpoint and should be recommended as the first-line treatment for Graves’ disease except in children and pregnant and breast-feeding women, though a 185 MBq dosage is often associated with a high percentage of persistence or relapse. RIT may not be recommended for Graves’ disease in adolescents because of the experience with the Chernobyl nuclear accident, which caused an increase in prevalence of thyroid cancer in adolescents as well as children\(^{25,26}\). The Chernobyl experience is, however, incomparable with RIT. Indeed, no corre-
lation between RIT and development of thyroid cancer even in adolescents has been reported. The high-fixed-dose RIT alone strategy showed the highest lifelong utility of 15.2, but with the highest lifelong cost, ¥154,459 (US $1,404) per patient (cost-effectiveness ratio: ¥10,162/utility). The initial administration of a high-fixed dose of $^{131}\text{I}$ results in inevitable, earlier and permanent hypothyroidism, which requires a lifelong l-thyroxin replacement. The long-term euthyroid state after RIT is a significant advantage in terms of cost and lifelong utility. The longer the duration, the lower the cost, and the higher the utility becomes. However, a low-fixed dose RIT alone strategy is often associated with a higher percentage of persistence or relapse, which decreases utility or quality of life.

The lifelong cost of the ATD plus RIT strategy varied with incidence of side effects of ATD. The 20% incidence was associated with the lowest cost, ¥78,391 (US $713), mainly because the 20% replacement with RIT reduced the cost of a lifelong supply of methimazole. The lifelong cost of US $713, which was discounted 5% in the future, is not expensive, when compared to the cost of a one-year supply of methimazole (15 mg daily, US $360, or 30 mg daily, US $720)\(^{[4]}\). Conversely, the 30% incidence of side effects increased the lifelong cost because of the increase in the number of RIT treatments at a relatively high cost.

The ATD therapy plus STT strategy was costly, ¥91,995 (US $836). STT for Graves’ disease is the surest means of achieving euthyroidism, and earlier, but surgery is expensive and requires hospital admission.

The subjects who underwent STT and responded to the questionnaire had no postoperative complications, such as hoarseness or symp-toms of hypoparathyroidism. However, the reason for the lower short-term utility in STT patients (0.92, 0.95) is thought to be cosmetic disfigurement, malaise, and numbness of the surgical scar. ATD therapy is aimed at preserving thyroid function. Patients on permanent ATD therapy are not completely cured. The reason short-term utility was lower in the ATD plus RIT strategy group (0.86 - 0.99) than in the RIT alone strategy group (0.93 - 0.98) is probably unstable symptoms, even if they were mild. Daily ATD therapy and seasonal adjustment of the dosage are cumbersome, and probably lowered the short-term utility. Patients with potentially life-threatening agranulocytosis were enrolled in our patient group. The Graves’ disease patient who developed sepsis secondary to agranulocytosis, had a short-term utility score of 0.2. If major complications of ATD are more frequent, short-term utility would be considerably lower in the ATD plus RIT or STT strategies.

Naturally, short-term utility greatly affected lifelong utility in our series. The lifelong (30 years) utility per patient was greatest in the group treated with the high-fixed dose RIT alone strategy, and lowest in the group treated with ATD plus RIT with a 1% incidence of side effects of ATD. A high-fixed dose RIT alone strategy achieves a stable state with replacement therapy earlier, and is probably a preferred one for Graves’ disease patients with complications such as heart disease, diabetes mellitus, neuromuscular disease, and neuropsychiatric syndromes.

4.2 Study limitations
In our series, patients in whom no remission had been achieved after ATD therapy continued to take ATD. However, the guideline in the
United States shows that Graves’ disease patients with relapse after medical treatment choose continuing medical therapy, RIT or surgery\(^{28,29}\). Indeed, a majority of Japanese hospitals cannot provide Graves’ disease patients with RIT. Only 11% of Japanese hospitals with nuclear medicine practice can afford to perform RIT\(^{30}\). Actually, it may be difficult to perform RIT alone strategy or RIT for all patients with relapse after ATD therapy in this day and age in Japan.

We adopted radioiodine-fixed-dose methods in our strategy, not radioiodine adjusted-dose methods. The difference in clinical outcome between the two methods is not significant according to the literature\(^{9}\).

A STT alone strategy was not included in our series. Many patients prefer non-surgical treatment for Graves’ disease. The STT alone strategy is actually impractical except in patients’ group with a very large goiter, a need for rapid restoration of thyroid function to normal, or a concurrent thyroid tumor. If most Graves’ disease patients were treated by STT, there would not be enough hospital capacity or sufficient surgical teams to perform the operations.

The effect of RIT on Graves’ ophthalmopathy is a matter of controversy\(^{31-33}\). RIT probably aggravates exophthalmos among Graves’ disease patients, but any worsening of orbitopathy by RIT is usually mild and temporary\(^{31,35}\).

5. Conclusion

A decision-tree analysis was designed on the basis of the 4 competing strategies of ATD therapy: (1) an ATD plus RIT strategy, (2) an ATD plus STT strategy (3) a low-fixed-dose RIT alone strategy, (4) a high-fixed-dose RIT alone strategy in order to determine their expected lifelong cost and utility in Graves’ disease patients. The cost-effectiveness ratio was lowest (¥5 008/utility) in a low-fixed-dose RIT alone strategy. A low-fixed-dose RIT alone strategy is preferred treatments in view of cost-effectiveness ratio, and RIT should be used more widely in Japan.

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要 旨

グレープス病に対する抗甲状腺剤、131I治療、甲状腺亜全摘術の費用効果分析

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グレープス病患者のアンケート調査に基づき，判断感度分析と関連する変動因子を用いて生涯の期待費用，効用値を計算することによって，グレープス病に対する抗甲状腺剤，131I治療，甲状腺亜全摘術の費用効果分析を行った。分析にあたって，（1）抗甲状腺剤と131I治療，（2）抗甲状腺剤と131I治療，（3）低線量（185 MBq）131I治療，（4）低線量（370 MBq）131I治療，の4群について検討した。生涯費用は低線量131I治療が最も低額で，高線量131I治療が最も高額であった。生涯効用値は高線量131I治療が最も高く，抗甲状腺剤と131I治療が最も低値であった。費用効果比は低線量131I治療が最も低く，¥5008/効用であった。結論として，費用効果分析上，低線量131I治療がグレープス病治療において最も優れており，広く普及すべき治療法と思われる。