Clinical Study

Thyroid-associated ophthalmopathy; quality of life follow-up of patients randomized to treatment with antithyroid drugs or radioiodine

Mirna Abraham-Nordling, Göran Wallin1,2, Frank Träsk3, Gertrud Berg4, Jan Calissendorff5, Bengt Hallengren6, Pavo Hedner7, Mikael Lantz8, Ernst Nyström9, Peter Åsman9, Göran Lundell10, Ove Töring11,12, and The Thyroid Study Group of TT 96†

Department of Clinical Sciences, Division of Surgery, Danderyd Hospital, Karolinska Institute, S-18288 Stockholm, Sweden, 1Department of Molecular Medicine and Surgery, Karolinska Institute, SE-141 86 Stockholm, Sweden, 2Department of Surgery, Örebro University Hospital, SE-70185 Örebro, Sweden, 3Department of Clinical Neurosciences, Karolinska Institute, St Erik Eye Hospital, SE-112 82 Stockholm, Sweden, 4Department of Oncology, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden, 5Department of Endocrinology, Radiumhemmet, Karolinska Institute, Karolinska University Hospital, SE-141 86 Stockholm, Sweden, 6Department of Endocrinology, Malmö University Hospital, SE-205 02 Malmö, Sweden, 7Department of Endocrinology, Lund University Hospital, SE-221 85 Lund, Sweden, 8Department of Endocrinology, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden, 9Department of Ophthalmology, Malmö University Hospital, SE-205 02 Malmö, Sweden, 10Department of Oncology, Radiumhemmet, Karolinska Institute, Karolinska University Hospital, SE-141 86 Stockholm, Sweden, 11Department of Clinical Research and Education, Karolinska Institute and 12Division of Endocrinology, Department of Internal Medicine, Södersjukhuset, SE-118 37 Stockholm, Sweden

(Correspondence should be addressed to M Abraham-Nordling; Email: mirna.abraham.nordling@ki.se)

†(Please see Acknowledgements)

Abstract

Objective: The objective of this study was to investigate quality of life (QoL) in patients with Graves’ disease treated with radioiodine or antithyroid drugs.

Design and methods: The design of the study consists of an open, prospective, randomized multicenter trial between radioiodine and medical treatment. A total of 308 patients were included in the study group: 145 patients in the medical group and 163 patients in the radioiodine group. QoL was measured with a 36-item Short Form Health Status Survey questionnaire (SF-36) at six time points during the 48-month study period.

Results: Patient who developed or got worse of thyroid-associated ophthalmopathy (TAO) at any time point during the 4-year study period (TAO group) had lower QoL when no respect was paid to the mode of treatment.

TAO occurred in 75 patients who had radioiodine treatment at some time point during the study period as compared with TAO in 40 medically treated patients (P<0.0009). Comparisons between the group of patients who have had TAO versus the group without TAO, in relation to treatments and time, showed significantly decreased QoL scores for the TAO groups at several time points during the study.

In patients without TAO, there were no differences in QoL related to mode of treatment.

Conclusions: The QoL in patients with Graves’ ophthalmopathy was similar in radioiodine and medically treated patients, but patients who developed or had worsening of TAO had decreased QoL independent of mode of treatment. Furthermore, patients with TAO recovered physically within 1 year but it took twice as long for them to recover mentally.

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Introduction

Hyperthyroidism is a common disease which affects 32.7–41.6 cases/100 000 per year in Sweden (1, 2). In the majority of patients, Graves’ disease is the cause, and thyroid-associated ophthalmopathy (TAO) is one of the main complications (3, 4).

Several studies have shown that TAO is the main reason for discomfort and decreased quality of life (QoL) (5–8).

We have previously observed an increased risk of TAO associated with radioiodine treatment of Graves’ hyperthyroidism in comparison to medical or surgical treatment in a randomized study, ‘Thyrotoxicosis 1983 (TT83)’ (9). In that study, patients in the radioiodine group received l-thyroxine (T4) only when biochemical hypothyroidism occurred, which may have affected the outcome (10–13). Therefore, we designed a new randomized study ‘Thyrotoxicosis 1996 (TT96)’...
between radiiodine and medical treatment of Graves’
hyperthyroidism, in which both study groups received
\( ^{131}I \) early after administration of radioactive iodine
\( (^{131}I) \) and after antithyroid drugs (ATDs) to prevent
hyperthyroidism. The increased risk of TAO associated
with \( ^{131}I \) treatment was reconfirmed (14). When the
TT96 study was planned in 1994–1996, we designed
the study to also address QoL aspects and added the
36-item Short Form Health Status Survey (SF-36)
questionnaire to the follow-up parameters. The reason
for that was in our original study (9), we had observed a
decreased mental score and vitality for all three
treatment modalities on a follow-up 2 years later (15).

We have also shown that all three treatment groups
had a lower QoL compared to an age-matched Swedish
reference population group at long-term follow-up at 17
years (16). However, a possible impact of TAO on the
QoL scores was not taken into account. In the present
study, we report the QoL results from our large
randomized study, TT96, in Graves’ patients treated
with radiiodine or ATD (14).

Materials and methods

Study design

The study was designed as an open, randomized,
prospective multicenter trial. Patients were randomized
to radiiodine (group I) or medical treatment (group M)
within each center(stratified randomization). Randomi-
ization was made in blocks over time and was performed
by the Oncological Centre at the Karolinska University
Hospital in Stockholm. (For more details, see Traisk
et al. 2009.)

The study was approved by the ethics committee of
the Karolinska Institute (Ref.: KI 96-096).

Patients

Inclusion criteria were as follows: age, 35–69 years;
symptomatic Graves’ hyperthyroidism; confirmation of
the diagnosis by serum TSH (\( \leq 0.1 \text{ mIU/l} \)) and elevated
tri-iodothyronine (T3) and/or free T4; thyroid uptake of
\( ^{131}I \); and radionuclide scans compatible with Graves’
disease, i.e. an even distribution of radionuclide.
Furthermore, the activity of an orally administered
dose of \( ^{131}I \) (as calculated to give the patient an
absorbed radiation dose of 120 Gy to the thyroid gland)
should not exceed 600 MBq, enabling the therapy to be
given on an outpatient basis (see formula in \( ^{131}I \)
section). This implied that patients with large goiters
were excluded. Patients with a previous history of
therapy with ATDs, \( ^{131}I \), or thyroid surgery were
excluded as well as patients with severe TAO requiring
treatment with corticosteroids at the time of inclusion.
This was done because concomitant steroid treatment
would limit the possibility to evaluate the effect of the
treatment for Graves’ disease on worsening or develop-
ment of TAO. Additional exclusion criteria were
incipient toxic crisis, coronary heart disease, pregnancy,
breast-feeding, or pregnancy planned within the
following 2 years. The total number of patients that
met the inclusion criteria is not known, but the reported
cases were 482. A total of 333 patients gave their
informed consent to participate and were enrolled in the
study. For ethical reasons, clinical data were not
documented for the patients who did not wish to
participate or did not meet the inclusion criteria. Of the
333 patients enrolled in the study, 20 patients were
excluded, 1 patient had an incorrect diagnosis (Hashi-
moto thyroiditis), 17 had no ophthalmological assess-
ment at randomization, and 2 had no follow-up visits.
These excluded patients had an average age of 50.1
years, the male/female ratio was 5/15; of 18 patients, 5
were smokers, and 2 were missing data. The number of
patients belonging to each center was as follows:
Gothenburg, 58; Lund, 40; Malmoe, 73; and Stock-
holm, 142 patients respectively.

Altogether, 313 patients were included in the study
group: 150 patients in the medical therapy group
(group M) and 163 patients in the radiiodine group
(group I). Twenty-two patients in the radiiodine-treated

Figure 1 Patients in which both eye score and SF-36 questionnaire
were available at baseline according to treatment \( (^{131}I) \) and medical
therapy) and presence of TAO at baseline or developed de novo
during the study.
Table 1 The presence or absence of thyroid-associated ophthalmopathy (TAO) at baseline or following treatment in the two treatment groups.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Without TAO</th>
<th>With TAO</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>105 (72.4%)</td>
<td>40 (27.6%)</td>
<td>145</td>
</tr>
<tr>
<td>Radioiodine</td>
<td>88 (54.0%)</td>
<td>75* (46.0%)</td>
<td>163</td>
</tr>
<tr>
<td>All groups</td>
<td>193</td>
<td>115</td>
<td>308</td>
</tr>
</tbody>
</table>

*P=0.0009, Pearson χ² test.

Follow-up by group I and group M respectively was as follows: at 1 year, 3 and 1%; at 2 years, 6 and 3%; and at 3 years, 10 and 9% respectively. At 4 years (i.e. after protocol for ophthalmological follow-up), 20% of the patients in both groups were still followed by ophthalmologists.

Treatment for Graves’ hyperthyroidism

Medical Methimazole was given 15 mg twice daily, and at day 14, 50 µg of l-T4 was added, and it was increased to 100 µg daily 2 weeks later.

At 6 weeks, the dose of l-T4 was adjusted to normalize the levels of serum T3 and free T4 and to bring TSH to <0.4 mIU/l. A slightly elevated serum-free T4 was accepted up to 20% above the upper normal limit. Beta-blockers were used for symptomatic treatment. Patients showing serious adverse reactions to methimazole received alternative treatment. Methimazole was replaced by 150 mg propylthiouracil three times daily in patients with minor adverse reactions.

ATD therapy was discontinued after 18 months with an additional month of l-T4 substitution of 100 µg daily, which thereafter was discontinued.

131I Beta-blockers were used as pretreatment to the radioidine therapy. The intention was to give one dose of radioactive iodine, aiming for an estimated absorbed radiation dose in the thyroid gland of 120 Gy. The administered activity was calculated using the following formula (10): Activity (MBq) = (23.4 × thyroid mass (g) × 120 (Gy))/(estimated uptake (0 h; %) × effective half-life (days)). The thyroid mass was assessed by thyroid scintigraphy and by palpation. Reference models of a thyroid gland were used to aid the assessment (30, 40, 50, and 60 ml). The effective half-life of 131I and the estimated thyroid uptake at 0 h were calculated from the initial 24 h thyroid iodine uptake and a new uptake test 4–9 days later, i.e. the same day the radioidine therapy was given. l-T4 substitution was administered with the same type of regimen as used in group M.

Follow-up by thyroidologist (endocrinologist or oncologist)

The patients were followed up by a thyroidologist four times in the first year and then one to two times yearly (endocrinologist or oncologist) where the treatment for hyperthyroidism was monitored by clinical assessment and laboratory evaluations. At the first visit and after 3, 12, 24, 36, and 48 months, they answered the Swedish version of the validated generic Medical Outcome Study (MOS) SF-36 questionnaire. If at any time TAO developed or deteriorated, the patients were referred to the ophthalmologist for additional eye examinations. (For details, see (14)).

Follow-up by ophthalmologist and SF-36

Within the first 2 weeks following enrollment, all patients were seen by an ophthalmologist and thereafter at 3, 12, 24, and 36 months as part of the study protocol and additionally if TAO developed. (For details, see (14)).

After 36 months, additional assessments were performed at the eye clinic upon referral by the thyroidologists or if the patients were followed up because of established TAO. Also, during the 4-year follow-up, patients with active TAO had eye assessments by ophthalmologists every 6 weeks until the condition had markedly improved. At each visit at the eye clinic, visual acuity, proptosis, eyelid retraction, eyelid swelling, chemosis, conjunctival redness, impairment of the eye movements, corneal ulceration, and optic nerve involvement were documented (see supplemental data of (14)). Eyelid retraction alone was not classified as TAO. Within each center, the majority of patients were followed by the same ophthalmologist throughout the study.

For the set criteria (worsening or development and improvement of TAO), two of the following four decisive factors were required (compared with baseline data): i) change in exophthalmometry readings of 2 mm or more; ii) improvement or deterioration of the patient’s eye movements between the four scoring levels (no impairment, clearly impaired, diplopia in the primary position, and fixation of the globe); iii) changes of visual acuity caused by optic neuropathy; and iv) changes in two of the three TAO activity measures (chemosis, eyelid edema, and conjunctival redness). The patients who did not meet the criteria of improvement or worsening or development of TAO were referred to as having no change of TAO.

SF-36

SF-36 QoL was measured with the Swedish version of the MOS SF-36 (17–20).
The questionnaire includes 36 items that can be classified into the following eight health status subscales: physical functioning, physical role limitations, bodily pain, general health perception, vitality, social functioning, emotional role limitations, and mental health. A standardized physical component summary (PCS) and a standardized mental component score were calculated (20). In SF-36, eight subscales are summary scales transformed to range 0–100, while the PCS and the mental component summary (MCS) are weighted scores, constructed to mean$Z50$ and s.d.$Z10$ (17–20).

**Statistical analysis**

The result from the SF-36 scores comprises of eight subscales, which are summary scales transformed to range 0–100, while PCS and MCS are weighted scores, constructed to mean = 50 and s.d. = 10 (17–20).

**Results**

Patients who had experienced development or worsening of eye problems at any time point during the 4-year study period (TAO group) had lower QoL estimated by the SF-36 questionnaire when no attention was paid to the mode of treatment. The TAO group at baseline already had a somewhat lower MCS score, although not statistically significant. Throughout the whole study period, the TAO group had lower MCS and PCS for the first 3 years (Fig. 2a and b).

To study the possible influence of treatment modality on the occurrence of TAO, we thus found that more patients ($n=75$) who had radioiodine treatment had experienced TAO at entry or at some time points during the study period as compared with the 40 medically treated patients ($P<0.0009$, Table 1). There were no differences in the results of the SF-36 scores between the two treatment groups. Figure 3 shows the MCS and PCS scores. It is evident from Fig. 3 that at diagnosis (month 0) of Graves’ disease, both groups had decreased QoL SF-36 score as compared with the Swedish reference population. The QoL scores increased in both treatment groups during the study. Already after 3 months, the physical component score reached the average for the Swedish reference population (score 50) and remained at this level throughout the study period (48 months; Fig. 3a). The mental component score showed some delay in both the radioiodine and medically treated groups to reach the average score of 50 not until 12 months. Thereafter, the mental component score remained rather constant for 3 years or at least until 48 months (Fig. 3b).

Comparisons between the two groups of patients without TAO showed no significant differences in QoL regardless whether they had been treated with radioiodine or ATDs.

Comparisons between the group of patients who have had TAO versus the group without TAO, in relation to
treatments and time, showed significantly decreased QoL (SF-36) scores for the TAO groups at several time points during the study (Table 2).

In the whole study group, the frequency of patients with more severe ophthalmopathy was highest at 1 year after enrollment, 11.2%) compared with 6.1% at baseline. Severe ophthalmopathy was denoted here as increase of proptosis of 3 mm or more and/or deterioration of eye motility compared to baseline data.

At the 1-year time point, there was no clear correlation association between the objective eye score and PCS and MCS. Neither were there any significant differences between those with eye scores above 3 or below 3 time points with respect to PCS and MCS.

### Table 2

Patients with thyroid-associated ophthalmopathy (TAO) and 36-item short form health status survey in relation to treatment group. The table shows, for both treatment groups, all time points during the study when patients with TAO as a group had a significantly decreased QoL compared with patients without TAO. Analyses were done for all time points, but only significant results are shown (Mann–Whitney U test).

<table>
<thead>
<tr>
<th>Treatment/time point</th>
<th>0 months</th>
<th>3 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
<th>48 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS</td>
<td></td>
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<tr>
<td>Radioiodine</td>
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</tr>
<tr>
<td>Medical</td>
<td>n=33, P=0.0323</td>
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<tr>
<td>MCS</td>
<td></td>
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<tr>
<td>Radioiodine</td>
<td>n=62, P=0.0187</td>
<td>n=66, P=0.0056</td>
<td></td>
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</tr>
<tr>
<td>Medical</td>
<td>n=33, P=0.0035</td>
<td></td>
<td></td>
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<tr>
<td>Physical functioning</td>
<td></td>
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<tr>
<td>Radioiodine</td>
<td>n=33, P=0.0111</td>
<td></td>
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<tr>
<td>Medical</td>
<td>n=19, P=0.0202</td>
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<tr>
<td>Bodily pain</td>
<td></td>
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<tr>
<td>Radioiodine</td>
<td>n=30, P=0.0174</td>
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<tr>
<td>Medical</td>
<td>n=34, P=0.0080</td>
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<tr>
<td>General health</td>
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<tr>
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<td>n=29, P=0.0363</td>
<td>n=35, P=0.0348</td>
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<tr>
<td>Medical</td>
<td>n=64, P=0.0220</td>
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<tr>
<td>Vitality</td>
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<tr>
<td>Radioiodine</td>
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<tr>
<td>Medical</td>
<td>n=19, P=0.0312</td>
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<tr>
<td>Social functioning</td>
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<tr>
<td>Radioiodine</td>
<td>n=62, P=0.0072</td>
<td>n=67, P=0.0326</td>
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<td>Emotional role</td>
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<tr>
<td>Radioiodine</td>
<td>n=67, P=0.0248</td>
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<tr>
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<tr>
<td>Radioiodine</td>
<td>n=62, P=0.0454</td>
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</tr>
<tr>
<td>Medical</td>
<td>n=35, P=0.0142</td>
<td>n=34, P=0.0190</td>
<td>n=27, P=0.0411</td>
<td></td>
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</tbody>
</table>

### Discussion

The patients were thoroughly and equally controlled in both treatment groups throughout the follow-up period. In addition, hypothyroidism was avoided by early addition of L-T4 in both treatment groups.

When no consideration of the mode of treatment was taken into account, it was clear that patients with TAO had a significantly decreased QoL for a considerable amount of time after treatment (Fig. 2a and b). This observation corroborated earlier finding by others when an eye-specific questionnaire had been used (6–8).

Hypothyroidism after radioiodine treatment has been considered to increase the risk of TAO. However, no such...
association could be revealed in a post hoc analysis of a randomized prospective study (21). Furthermore, in the present study where hypothyroidism was avoided, an increased risk of TAO associated with radioiodine was still observed. The study thus supported the concept of radioiodine as an independent risk factor for development or worsening of TAO as we had proposed earlier (9, 22). The study also showed that QoL was rather equal in both treatment groups when no attention was paid to the possible influence of TAO (Fig. 3a and b). Interestingly, the improvement in mental QoL was somewhat slower to normalize as compared with the physical performance capacity. In previous studies, we have observed that patients with Graves’ hyperthyroidism had lower mental QoL scores at follow-up after treatment (16). Most likely, the negative influence on normal brain functions by the hyperthyroid phase before treatment may have taken a considerable amount of time to resolve after start of treatment. According to Fig. 3b, it took 3 months for the radioiodine group and almost a year for the medically treated group to reach the average of 50 points for the Swedish reference population. The patients were substituted to have a TSH value <0.4 mIU/L and whether this was of importance for the rather slow improvement in mental QoL is open to speculation.

The observation that the QoL scores were rather equal in both treatment groups was a positive outcome of treatment of such a common and serious disease. The finding also corroborates our previous results from TTS3 that the mode of treatment did not significantly affect the QoL as estimated by the generic questionnaire SF-36 (16, 23). However, in this analysis, no attention was paid to when in the study period eye problems occurred or the clinical course of TAO. This could potentially have equaled out possible influences of TAO on SF-36 scoring. We therefore performed a subsequent analysis of when during the follow-up period the TAO occurred in each treatment group (Table 2). Patients with TAO generally had significantly lower QoL scores as compared with patients without TAO at several time points, but no consistent treatment- or time-related pattern could be found. However, patients without TAO never had lower QoL compared with TAO patients. Patients with TAO, on the other hand, had lower SF-36 scores independent of the mode of treatment.

It is important to keep in mind that the material was analyzed in the way that once a patient experienced TAO that particular patient was included in the TAO group without regard to the time point during the study the event occurred. Therefore, we have analyzed the relation between the SF-36 score and TAO at the 1-year follow-up where the TAO patients had the highest eye scores (14). This was done in an attempt to explore whether the SF-36 questionnaire at all time points reflected the influence of eye problems on QoL, since it is possible that the patients’ response to the questions in SF-36 may have reflected not only the probable eye problems but also the Graves’ disease (GD) in itself. The 1-year follow-up was selected since previous studies have shown that the majority of patients felt rather well at 1 year.

The result of this analysis showed that the SF-36 due to its generic properties is not an optimal instrument for measuring QoL-related issues in this population. A caveat of this study therefore is the possibility that the SF-36 questionnaire does not capture all the approriate quality-of-life issues that are relevant for patients who have had GD. Although the SF-36 is used extensively, it has not been specifically evaluated in a population of GD patients, but neither have other disease-specific instruments. However, the Hyperthyroidism Complaint Questionnaire developed by Fahrenfort et al. (4) has approached this issue with respect to long-term complaints. We however, decided to use the SF-36, for the following important reasons. The SF-36 questionnaire has been extensively evaluated in a large age-matched Swedish reference population, allowing us to make an appropriate comparison with our study group. Another caveat of the study is that it did not cover the whole spectrum of eye problems associated with Graves’ ophthalmopathy since patients with the most severe TAO, who at inclusion required steroid treatment, were not included.

Conclusions

The QoL in patients with Graves’ ophthalmopathy was similar in radioiodine and medically treated patients, but patients who developed or had worsening of TAO had decreased QoL independent of mode of treatment. Furthermore, patients with TAO recovered physically within 1 year, but it took twice as long for them to recover mentally. The QoL in patients without TAO seemed to be independent of mode of treatment.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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References


5 Gerding MN, Terwee CB, Dekker FW, Koornneef L, Prummel MF & Wiersinga WM. Quality of life in patients with Graves’ ophthalmopathy is markedly decreased: measurement by the medical outcomes study instrument. Thyroid 1997 7 885–889. (doi:10.1089/thy.1997.7.885)


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