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Value of Thyroid Follow-up Registers

MELCHER FALKENBERG,¹ OVE R. NILSSON² and ULF ROSENQVIST²

¹Community Health Centre, Kisa, Department of Preventive and Social Medicine, University of Linköping and ²Department of Internal Medicine, University Hospital, Linköping, Sweden.

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In this study from a county in southern Sweden 269 of 271 patients (99.3 %) treated with radioiodine for hyperthyroidism over a two-year period were followed up five years later. The routine procedures at hospital clinics and primary health care centres were studied. A high number of toxic multinodular goitre ($n=113$; 42.0 %) and toxic adenoma ($n=76$; 28.3 %) emerged, 80 patients (29.7 %) had toxic diffuse goitre (Graves's disease). During the five-year follow-up the cumulative incidence of hypothyroidism in the various goitre groups was 10.7 %, 23.9 %, and 57.5 % respectively. Altogether 76 patients (28.3 %) were diagnosed hypothyroid. Nine patients were lost to regular follow-up; elevated TSH and low or normal T4-concentrations were found in two of them. We propose a register system to enable detection of thyroid dysfunction after radioiodine treatment and other thyroid patients in primary health care.

Key words: radioiodine therapy, hyperthyroidism, hypothyroidism, follow-up register.

Melcher Falkenberg, MD, Kisa Community Health Centre, S-590 40 Kisa, Sweden.

Radioiodine treatment of hyperthyroidism is safe and effective, and it is well established, especially in the treatment of the middle-aged and the elderly (1). A major risk is that iatrogenic hypothyroidism may develop sooner or later. Owing to a reported incidence of hypothyroidism of up to 80 % after six years, lifelong follow-up has been recommended (2). Detailed follow-up registers, possibly computer assisted, have also been advocated (3, 4, 5).

The hitherto highest reported prevalence of hyperthyroidism (Medline 1986) was recently published after screening a primary health care district, Kisa (6, 7) in the county of Östergötland, which is known to be a goitre region (8). All patients treated for hyperthyroidism are now registered for regular follow-up at the primary health care centre. The present survey was extended to cover the whole county in order (i) to find out whether patients given radioiodine treatment for hyperthyroidism were subject to any form of planned follow-up, (ii) to evaluate manual registration of patients treated with radioiodine and subsequently followed up in primary health care, (iii) to estimate the overall

thyroid morbidity after radioiodine therapy, and (iv) to discuss the value of a follow-up register for patients with thyroid disorder in primary health care.

MATERIAL AND METHODS

Altogether 271 patients from the county of Östergötland (392 428 inhabitants), with clinically and biochemically confirmed hyperthyroidism who had been given radioiodine treatment at the University Hospital, Linköping during 1979 and 1980, were followed up five years later. Patients were identified from the records of the Radiological Department. Of the 271 patients, 269 (99.3 %) were investigated (Table I). The mean age was 70 years (range 35-89) at the time of treatment, and the male/female ratio was 1:8. The diagnoses, toxic diffuse goitre (TDG, Graves's disease), toxic multinodular goitre (TNG), and toxic uninodular goitre (toxic adenoma, TA), were confirmed by studying clinical records and the standardized radioisotope scintigraphies (¹³¹I, 1.11 MBq). Of the patients 107

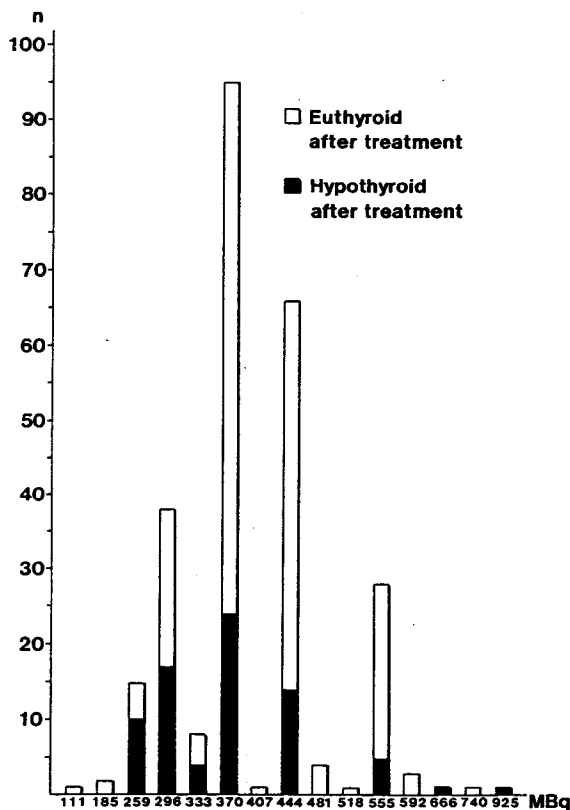


Fig. 1. Number of patients with hyperthyroidism treated with radioiodine and those who during a five-year period developed hypothyroidism, distributed according to dose.

(39.6%) had previously been treated for hyperthyroidism (22 by surgery, 37 with radioiodine, and 48 with antithyroid drugs). A further 13 patients had previously been operated on for non-toxic nodular goitre. Seven patients with TDG had ophthalmopathy. Fig. 1 shows the radioiodine doses used. Ten (3.7%) patients required a second dose of radioiodine because they were still hyperthyroid one year after the first dose; two of these required a third dose.

Patient records were studied at six hospital clinics and 19 primary health care centres regarding follow up and death. One hospital clinic and one primary health care centre (Kisa) used a separate register for patients treated with radioiodine to facilitate annual follow up. At the end point five years after treatment, 25 patients were followed up from these records; all other follow ups were integrated in the general register system. Thyroid function was evaluated by the clinical findings and laborato-

Table I. Women and men followed up five years after radioiodine treatment given over a two-year period

Age	Women n	Men n	Total
35-39	2		2
40-44			
45-49	5		5
50-54	6	1	7
55-59	11	2	13
60-64	28	5	33
65-69	57	10	67
70-74	50	6	56
75-79	51	6	57
80-84	21	4	25
85-89	4		4
Total	235	34	269

ry tests for serum thyroxine (T4), triiodothyronine (T3) and serum thyreotropin (TSH).

The criterion for diagnosing hyperthyroidism was the raised level of serum-thyroxine and/or triiodothyronine. The criteria for primary hypothyroidism was the raised level of thyroid-stimulating hormone and low serum thyroxine.

Special interest was paid to follow-up and its reliability. At the Kisa centre a manual register for patients given radioiodine treatment has been in use since 1978, and it now covers 51 patients diagnosed 1978-1985. Its main function has been to signal when examination is due. The register has hitherto proved useful in detecting insidious onset of hypothyroidism in eight (15.7%) cases, and has ensured adequate replacement therapy.

RESULTS

Of the 269 patients included in the survey, 80 (29.7%) had TDG, 113 (42.0%) had TNG, and 76 (28.3%) TA, at the time of treatment.

Of the patients, 76 (28.3%) developed hypothyroidism during the five-year period after radioiodine treatment. The cumulative incidence of hypothyroidism in the various groups was TDG 57.5%, TNG 10.7%, TA 23.0% (Fig. 2). At the five-year follow-up 209 patients (77.7%) were alive (TDG 63, TNG 88, TA 58), and among these 67 (32.1%) developed hypothyroidism.

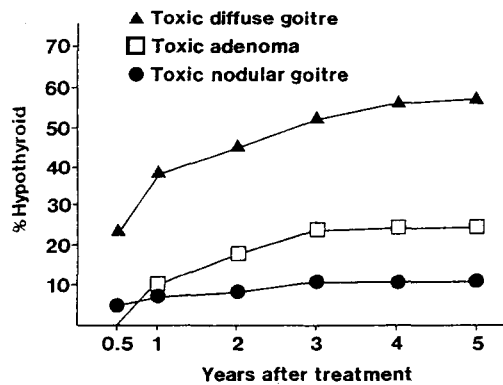


Fig. 2. Cumulative incidence of hypothyroidism after radioiodine therapy.

Sixty patients were dead after five years (mean survival time after radioiodine treatment 2.3 years; SD 1.2 years), and the incidence of documented hypothyroidism among them was nine (15%). Recurrence of hyperthyroidism after a period of normal thyroid function without drugs was noted in two patients, and these received a second dose of radioiodine. The incidence of established hypothyroidism following radioiodine treatment was not related to the dose (Fig. 1).

Most patients were examined annually. Five years after treatment 44% were seen at a primary health care centre and 56% at a hospital clinic. Nine patients (4.3%) were lost to follow-up five years after treatment; they were evenly distributed between hospital clinics ($n=5$) and primary health care ($n=4$). None of the patients lost to follow-up attended the clinic or health care centre using a special follow up register. The reason for failure in making regular follow-up examinations was in most cases lack of communication between the hospital clinic and the primary health care centre. These nine patients did not realize the need for lifelong follow-up; after information they underwent special clinical examination with determination of T4 and TSH. Two had biochemical evidence of hypothyroid function (elevated TSH and low T4); but no clinical sign of hypothyroidism.

DISCUSSION

Like other investigators we found a high incidence of hypothyroidism after radioiodine treatment. After ablative treatment with 555 MBq (15 mCi) ra-

dioiodine, Kendall-Taylor et al. reported an incidence of hypothyroidism of 64% after one year and of 80% six years after treatment (2). Low-dose radioactive iodine therapy in patients with Graves's disease resulted in an incidence of hypothyroidism of 12% at one year and a cumulative incidence of hypothyroidism of 76% after 11 years (9). The average dose in our patients can be considered to be somewhere between the doses used in the other studies mentioned. The prevalence of TNG and TA in our series (42.0% and 28.3%) is notably higher than reported by Kendall-Taylor (4.8% and 0%). We saw many cases of hypothyroidism after radioiodine treatment, even in patients with TNG, although the incidence was lower than among patients with Graves's disease, many of whom develop hypothyroidism after radioiodine treatment (2, 9). The appearance of hypothyroidism five years after radioiodine treatment among patients with TA is in accordance with what has been reported by Goldstein & Hart—25% (10). However, uncertainty regarding the classification exists due to lack of histopathology in our study. We find it important to follow up all patients after radioiodine treatment, irrespective of the cause.

We also observed that there is a risk of hypothyroidism regardless of the dose of radioiodine. Transient hypothyroidism may occur during the first six months after treatment, and it has been recommended that thyroxine replacement be withheld for two months unless symptoms are severe (11). We do not know whether this has happened in the present series. Patients with raised plasma TSH develop overt hypothyroidism at the rate of two to five per cent per year, and such patients need to be seen more often than those with normal plasma TSH (12).

What is the most effective way of ensuring surveillance over many years? Responsibility can be assigned to a hospital clinic or to a primary health care centre, and special registers can be set up with or without computer assistance: or the patient could be given the responsibility of contacting his doctor. Computer-assisted registers operated from endocrine clinics, such as the Scottish Automated Follow-up Register (4, 5, 13) and that described in the Birmingham study (3), have proved reliable, efficient, and economical. On the other hand critical voices have advocated supervision of patients who ought to accept some degree of responsibility for their own well-being (14). Patients at risk of

developing hypothyroidism do need active supervision if surveillance is to be adequate, but it is also important to avoid a large scale unproductive follow-up regime. The nine patients lost to follow-up did not attend a clinic or health care centre using a special register, a circumstance that could suggest advantages in such a system.

The long term follow up of patients with chronic disease is an essential part of the epidemiological function of primary health care (15). The manual register for patients given radioiodine treatment for hyperthyroidism and followed up at Kisa primary health care centre has proved effective without extra cost. We have found no difference in efficiency between hospital and primary health care follow-up. Manual records at the primary health care centres will shortly be replaced by computer-assisted registers; a manual register for thyroid dysfunction could be a part of such a system. Population-based registers will ensure adequate follow-up each time the patient attends the centre. If he moves, medical records should be transferred to his new health care centre.

We suggest that register functions in primary health care of patients with thyroid dysfunction and at risk of developing hypothyroidism should embrace the following categories:

1. Patients given radioiodine treatment for hyperthyroidism (1, 2, 9, 16).
2. Patients treated with antithyroid drugs (1).
3. Patients with autoimmune thyroiditis as indicated by thyroid hormone and thyroid antibody determinations (17).
4. Patients treated surgically (18, 19, 20).

Another group that could be included is patients on thyroid replacement therapy. Two recent studies support this suggestion. At an endocrine clinic, 70% of all patients who had been prescribed life-long thyroxine replacement therapy were found to be inadequately treated for one reason or another, including non-compliance, errors in prescribing or dispensing, or change in drug requirements (13). Jones et al. reported that 13% of patients followed up by a general practitioner were taking their medicine improperly, and showed serum thyroxine levels indicating hypothyroidism (5). These two studies indicate an obvious need for follow-up of patients on thyroxine replacement therapy. It may, however, be possible to improve results by con-

vincing the patient of the need to take his medications conscientiously (14), when necessary under medical supervision.

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