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Papillary and Follicular Thyroid Carcinoma

Individualization of the Treatment According to the Prognosis of the Disease

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Abstract—*A retrospective study of a continuous series of 152 patients is presented: the patients were treated between 1 January 1955 and 31 December 1981 for a papillary or a follicular thyroid carcinoma.*

The prognostic index, proposed by the EORTC Thyroid Cancer Cooperative Group in 1979, was calculated for each patient. According to the survival curves and recurrences after treatment, the study shows a clear-cut difference in prognosis if the prognostic index is below 50 or is equal to or above 50. This observation supports the proposal of minimal treatment for less aggressive tumors and extensive treatment for the high risk patients.

The actual treatment plan is: (1) total lobectomy when the tumor is unilateral and the prognostic index below 50, but total thyroidectomy in the other cases; (2) lymph node surgery only in cases of node involvement. Instead of a radical neck dissection, a more conservative procedure should be performed, removing the lymphatic chains and preserving the sterno-cleido-mastoid muscle, the internal jugular vein and the spinal accessory nerve; (3) no postoperative radioiodine for low risk patients with complete removal of the tumor; (4) postoperative thyroid hormone at doses suppressing secretion of TSH for all patients.

INTRODUCTION

CONTROVERSY remains on the extent of surgery for papillary and follicular thyroid carcinoma. The main questions are:

1. With gross tumor in one single lobe, is total thyroidectomy mandatory or is total lobectomy an adequate procedure?
2. When should cervical node dissection be done and what should be the extent of the surgical procedure?

Without any controlled clinical trials in the available literature, these questions have not been answered yet and extreme therapeutic attitudes are still proposed by surgeons.

This might probably be explained by the variety of the natural history in differentiated thyroid carcinoma. Several factors have been recognized to be of prognostic significance at presentation: age and sex of the patient, histology of the lesion, extent of the primary tumor, presence or absence of distant metastases and lymph node status. Therefore, it seems logical to adapt the treatment according to the risk of developing recurrent disease and/or metastases. Minimal surgery would be advised for less aggressive tumors and more extensive surgery for the poor risk patients.

Frazell [1], in 1976, already emphasized the need for individualized treatment of papillary thyroid cancer. Block [2], in 1981, made the same statement. Beahrs [3], in 1984, noted that the well-differentiated tumors, at the Mayo Clinic, are treated by conservative measures but that the operation may be more extensive for more aggressive lesions.

Mazzaferri and Young [4], in 1981, analyzing retrospectively data from 576 patients with papillary thyroid cancer, found that treatment with total thyroidectomy, postoperative radioiodine and thyroid hormone resulted in the lowest recurrence and mortality rates, except in patients with primary tumors smaller than 1.5 cm in diameter. For the latter, less than total thyroidectomy and postoperative therapy with thyroid hormone alone gave results which did not differ statistically from those achieved with more aggressive therapy. The same authors also mentioned that no statistically significant differences in recurrence or death rates were found

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among the three groups in whom lymph nodes were treated differently: no lymph node surgery, simple excision of the nodes or neck dissection, either radical or modified, even when the nodes were invaded.

Cady [5], reporting in 1981 the 40-year experience of the Lahey Clinic on 953 patients with thyroid carcinoma, considered that low-risk patients, which means men younger than 40 years of age and women less than 50 years with follicular or papillary carcinoma, should be treated conservatively since the risk of death is currently not higher than 1.5%: generally, the proposed treatment is lobectomy for the primary and limited or modified neck dissection if metastatic lymph nodes are palpated. For this author, the other cases are considered as high-risk patients and should be treated more aggressively, since recurrence rates may be high, and risk of death from disease may reach 15–20%.

Duncan and McCord [6] proposed, in 1983, to treat patients with differentiated thyroid carcinoma using a selective surgical approach based on criteria classifying patients into high- and low-risk subgroups, the categorization being based on the patient's age, the size and invasiveness of the tumor, and the presence or absence of distant metastatic disease: aggressive lesions should be treated by total thyroidectomy and low-risk lesions by simple lobectomy.

In 1966, the European Organization for Research and Treatment of Cancer (EORTC) Thyroid Cancer Cooperative Group began a registry of data on patients with thyroid carcinoma. Entry into this data set was continued until 1977, after some 1183 patients from 23 hospitals from various European countries had been registered. A study was published in 1979 by this group [7], after reexamination of the relative importance of the prognostic factors in 507 of these patients having the complete information needed for the analyses and assessment, by multivariate statistical analyses, of their importance when they are allowed to act together. A simple scoring system was devised for assigning patients to prognostic risk groups. The scoring system was presented as a prognostic index (Table 1) and five risk groups were defined, the marked differences in the 5-year survival curves of each of these groups demonstrating the validity of the groups formed in this manner.

Since 1975, we have decided to minimize the treatment for patients younger than 40 years of age with differentiated thyroid carcinoma. After publication of the EORTC study, we have thought that the use of the prognostic index might help choosing the treatment more accurately.

To try to substantiate this hypothesis, we studied retrospectively a continuous series of patients with papillary or follicular thyroid carcinoma treated in the Head and Neck Surgical Department of the Institut Jules Bordet.

Table 1. EORTC proposed prognostic index, obtained by calculation of the sum of the following

Age at diagnosis in years	
+12	if male
+10	if principal cell type is follicular less-differentiated
+45	if principal or associated cell type is anaplastic
+10	if T extension beyond the gland capsule
+15	if there is one distant metastatic site
+30	if there are multiple distant metastatic sites
=	Total score

MATERIALS AND METHODS

From 1 January 1955 to 31 December 1981, a thyroidectomy for cancer was performed in 152 patients (110 females and 42 males) with a mean age of 46 years (extremes: 7 and 81 years). All patients were previously untreated.

All the cases were classified according to histology, and clinical status and EORTC prognostic index (Table 2).

The prognostic index was calculated for each case and patients were divided in two groups according to this index: low-risk when the prognostic index was below 50 and high-risk if it was equal to or above 50.

Four types of operations were used, usually a total thyroidectomy or a total lobectomy. Occasionally, a subtotal thyroidectomy was performed, i.e. bilateral subtotal lobectomies in continuity with an isthmusectomy, preserving small amounts of posterior thyroid tissue and the attached parathyroid glands, on each side of the trachea. The last type of surgery encountered in this series consisted of a total lobectomy on the tumor side in continuity with an isthmusectomy, plus a portion of the adjacent contralateral lobe.

In order to compare the total thyroidectomy group against the total lobectomy group for unilateral tumors (without metastasis at presentation), Cox analysis was performed [8] taking first, all the patients together then, separately, each of the two prognostic categories (i.e. less than 50 after the scoring index and greater or equal to 50). The model included the prognostic index taken as a continuous variable and the type of surgery.

The survival curves were estimated, according to the actuarial method [9], separately for the low-risk and for the high-risk patients, and were compared

Table 2. Patient characteristics

	Number	Age	
		Mean (±S.D.)	Range
Histology			
Papillary carcinoma	103	45 (±16)	7–80
Follicular carcinoma			
well differentiated	12	44 (±21)	8–81
moderately differentiated	37	52 (±14)	27–77
Clinical status			
No evidence of regional or distant metastases	100	47 (±14)	17–81
With regional lymph node invasion, no metastases	38	40 (±18)	7–77
With distant metastases at presentation	14	63 (±17)	8–80
Prognostic index			
<50	70	33 (±11)	7–49
≥50	82	59 (±10)	41–81

to those of the whole population of the same mean age (Figs. 1 and 2) [10].

Serum calcium levels were routinely determined before and after operation.

Nine patients were lost to follow-up, respectively, 2 and 4 months and 2, 3, 6, 7, 9, 17 and 17 years after surgery.

RESULTS

The distribution of the various surgical techniques, according to the type of primary tumor and to the prognostic index, is displayed in Table 3. For the adjacent neck, there were 31 radical neck dissections, five modified neck dissections and two simple excisions of nodes. In 100 instances there was no lymph node surgery.

There were two local recurrences in the thyroid gland, nine cervical lymph node metastases and 16 distant metastases, among 139 patients without distant metastases at the time of first treatment.

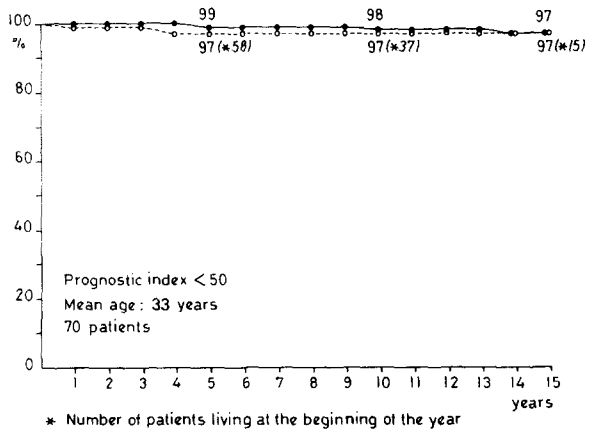

Fig. 1. Actuarial survival curve of the 70 low-risk patients (dotted line) compared to that of the population of normal subjects (continuous line). Figures on the curves are the percentage living at the beginning of the year; figures between the brackets are the number of patients at those corresponding times.

For the 70 low-risk patients, follow-up showed that survival curves were almost the same for the patients and for the whole population, whatever the treatment had been. Among those 70 patients, seven had recurrent disease after primary treatment but only one, a woman 49 years old, died with disease, 19 years after treatment: she was the only case who was not cured by subsequent treatment.

For the 82 high-risk patients, survival was distinctly inferior to that of the whole population. Thirteen patients had distant metastases at the time of initial treatment: they all died with disease. Among the 69 high-risk patients without distant metastases, recurrent disease was found in 15 and was successfully treated only in two, while the 13 other patients died from disease.

Permanent postoperative hypoparathyroidism was found in 13 patients: all of them had been treated by total thyroidectomy.

After adjustment for the prognostic index, the Cox

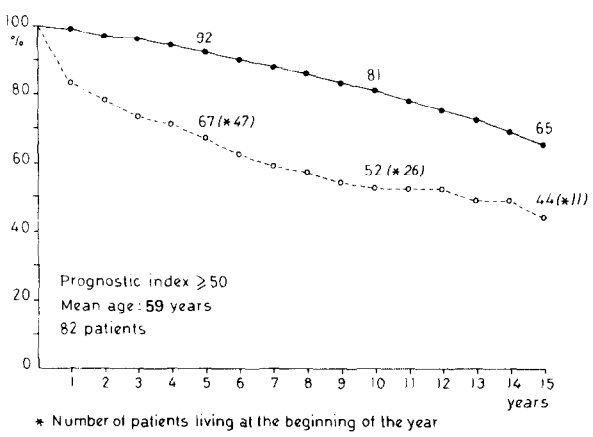

Fig. 2. Actuarial survival curve of the 82 high-risk patients (dotted line) compared to that of the population of normal subjects (continuous line). Figures on the curves are the percentage living at the beginning of the year, figures between brackets are the number of patients at those corresponding times.

Table 3. Type of surgery for thyroid gland

Surgery for thyroid gland	Number of patients						Total
	Prognostic index <50			Prognostic index ≥50			
	Unilateral tumor	Tumor of the isthmus	Bilateral tumor	Unilateral tumor	Tumor of the isthmus	Bilateral tumor	
<Total lobectomy	1	1	—	1	2	1	6
Total lobectomy	26	—	—	17	1	—	44
>Total lobectomy and< total thyroidectomy	2	—	—	5	1	—	8
Subtotal thyroidectomy	6	—	—	7	1	1	15
Total thyroidectomy	27	3	4	39	3	3	79

Table 4. Cox model (prognostic index and type of surgery)

	β	Standard deviation	*P* value
EORTC index	0.056	0.012	<0.0001
Type of surgery	1.22	0.51	0.01

model demonstrated a significantly better prognosis after conservative surgery in the overall population ($P = 0.01$) and in patients with a prognostic index greater or equal to 50 ($P = 0.023$) (Table 4 and Fig. 3). This was not demonstrated in the <50 prognostic index group ($P = 0.08$) (Fig. 4).

DISCUSSION

We are not able to demonstrate that the results of total lobectomy are different from those of total thyroidectomy, not only because our study was not prospective but also because our previous policy was to perform routinely total thyroidectomy for thyroid cancer. Total lobectomy was therefore mostly performed in recent cases or when the tumor

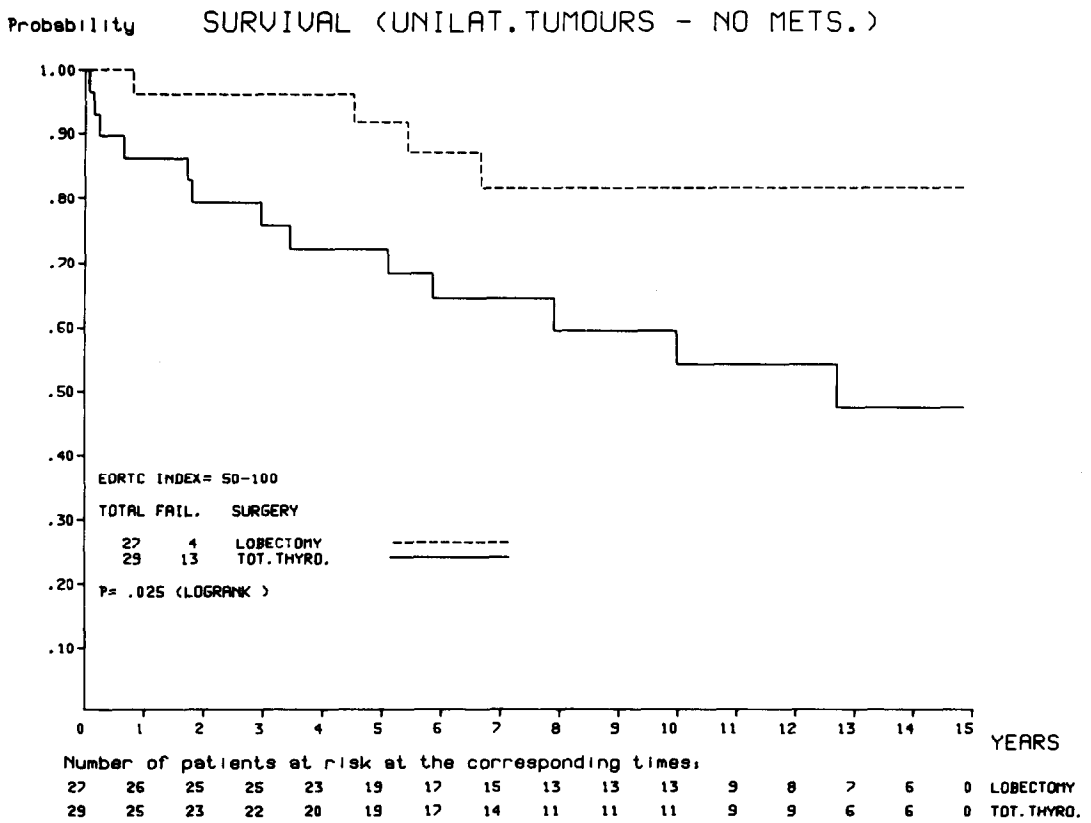

Fig. 3. Survival curves of the 27 lobectomized patients (dotted line) versus that of the 29 total thyroidectomies (continuous line) in the index-group greater or equal to 50, for unilateral tumors without metastases at presentation.

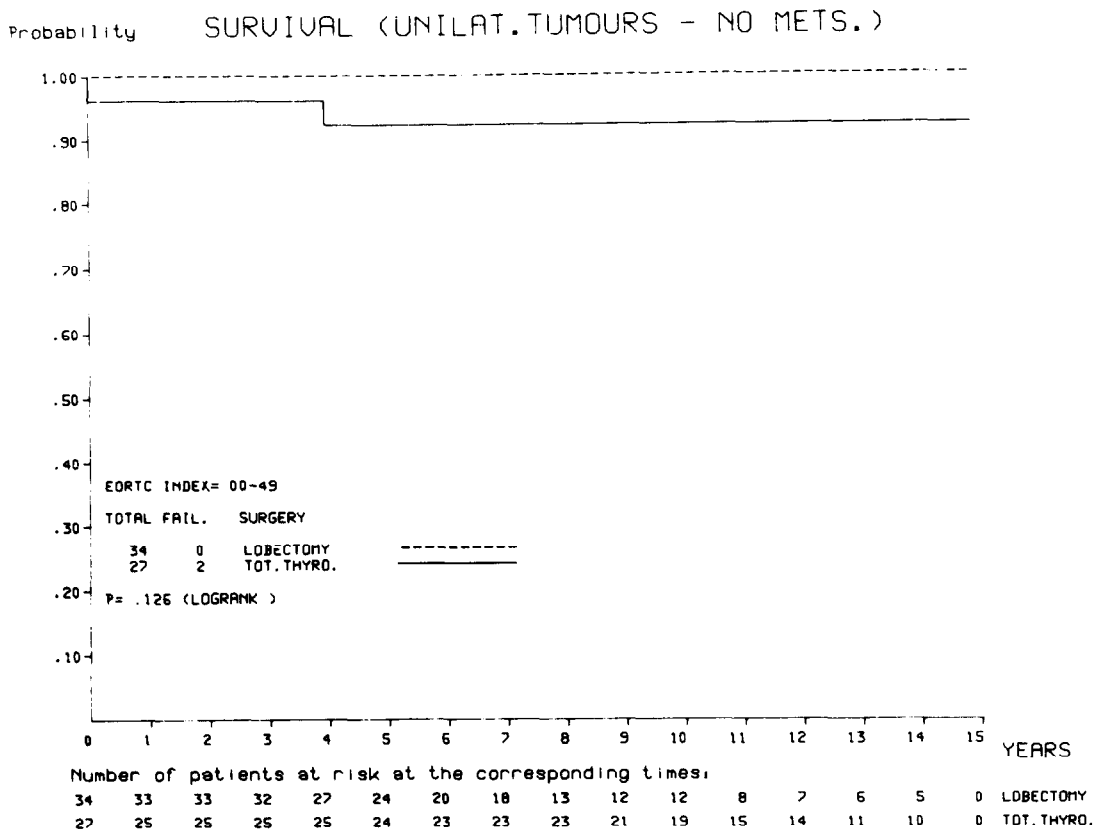

Fig. 4. Survival curve of the 34 lobectomized patients (dotted line) versus that of the 27 total thyroidectomies (continuous line) in the index-group inferior to 50, for unilateral tumors without metastases at presentation.

was small or undiagnosed on frozen section examination of the specimen.

The problem is the same for surgery of the regional lymph nodes. Our previous policy was to operate only in case of node involvement and, if so, to perform a radical neck dissection, but we are now in favor of a modified procedure, preserving the sterno-cleido-mastoid muscle, the internal jugular vein and the spinal accessory nerve.

Nevertheless, the retrospective study of our series shows a clear-cut difference in prognosis if the prognostic index is below 50 or is equal to or above 50 (Figs. 1 and 2).

It is not surprising that Cox analysis did not disclose any difference of prognosis after conservative versus extensive surgery in the <50 index group: the natural history of the well differentiated tumors in this particular group of patients is so favorable that no differences in prognosis might ever be disclosed, even with a follow-up of more than 20 years. This observation gives support to our hypothesis: less morbid management should be chosen in this category.

On the other hand, it could be wondered why there was no better survival after a more extensive treatment in the ≥50 index group. In that regard, we propose two possible explanations: first, the aggressiveness of the disease in that group of patients will be prominent whatever the local treatment might be, secondly, in a non-prospective, non-randomized study, some unmeasured prognostic variables might influence the outcome and therefore conclusions drawn from this analysis must be somewhat tentative. Our first statement does not imply that one should not do a total thyroidectomy in those patients with an index ≥50. Indeed, it is mandatory to perform an extensive surgical resection for those in order to avoid local problems and to give a better chance of effectiveness with radioiodine used as diagnostic or as therapeutic agent.

Considering these results, the higher frequency of hypoparathyroidism after total thyroidectomy and the utility, for high-risk patients, of complete removal of neoplastic foci and of postoperative whole body scan with radioactive iodine, we feel that the treatment of choice is total lobectomy, when the tumor is clinically unilateral and the prognostic index below 50, but total thyroidectomy in the other cases.

Furthermore, we still do not see any reason for lymph node surgery in patients without palpable cervical metastases. For the other patients, we propose to perform, instead of a radical neck dissection, a more conservative procedure, removing only the lymphatic chains, certainly for low-risk patients and probably also for the other.

Finally, we consider that all patients should be treated by thyroid hormone at doses suppressing secretion of TSH and that postoperative radioiodine

should not be given to low-risk patients with complete removal of the tumor.

We are fully aware that follow-up should be continued for several decades in young people due to the high incidence of multicentric lesions in papillary cancer and the possible anaplastic transformation of differentiated thyroid carcinoma in older patients.

Nevertheless, we consider that our treatment schedule, which was started in 1980 and was also adapted by Colon and Mayer [9] in 1981, is worthwhile because it allows to adapt the therapy to the prognosis of the disease which is one of the main goals of treatment of cancer.

REFERENCES

1. Frazell EL. The need for individualized treatment. In: Varco, Delaney, eds. *Controversy in Surgery*. Philadelphia, Saunders, 1976, 171–175.
2. Block MA. Primary treatment of well-differentiated thyroid cancer. *J Surg Oncol* 1981, **16**, 279–288.
3. Beahrs OH. Surgical treatment for thyroid cancer. *Br J Surg* 1984, **71**, 976–979.
4. Mazzaferri EL, Young RL. Papillary thyroid carcinoma: a 10 year follow-up report of the impact of therapy in 576 patients. *Am J Med* 1981, **70**, 511–518.
5. Cady B. Surgery of thyroid cancer. *World J Surg* 1981, **5**, 3–14.
6. Duncan TD, McCord D. Thyroid carcinoma: criteria in selection of patients for total and subtotal thyroidectomy. *J Natl Med Assoc* 1983, **75**, 401–404.
7. Byar DP, Green SB, Dor P *et al.* A prognostic index for thyroid carcinoma. A study of the EORTC Thyroid Cancer Cooperative Group. *Eur J Cancer* 1979, **15**, 1033–1041.
8. Cox DR. Regression models and lifetables (with discussion). *J R Stat Soc B* 1972, **34**, 187–220.
9. Berkson J, Gage RP. Calculation of survival rates for cancer. *Proc Mayo Clin* 1950, **15**, 270–286.
10. Statistiques démographiques, Institut National de Statistique, 1000 Bruxelles, 1979, pp. 22–24.
11. Colon J, Mayer M. Facteurs pronostiques du cancer thyroïdien. Incidence sur l'attitude thérapeutique. *Bordeaux Méd* 1981, **14**, 1321–1326.