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Papillary Thyroid Carcinoma Managed at the Mayo Clinic during Six Decades (1940–1999): Temporal Trends in Initial Therapy and Long-term Outcome in 2444 Consecutively Treated Patients

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Abstract. It is uncertain whether more extensive primary surgery and increasing use of radioiodine remnant ablation (RRA) for papillary thyroid carcinoma (PTC) have resulted in improved rates of cause-specific mortality (CSM) and tumor recurrence (TR). Details of the initial presentation, therapy, and outcome of 2444 PTC patients consecutively treated during 1940–1999 were recorded in a computerized database. Patients were followed for more than 43,000 patient-years. The 25-year rates for CSM and TR were 5% and 14%, respectively. Temporal trends were analyzed for six decades. During the six decades, the proportion with initial MACIS (distant Metastasis, patient Age, Completeness of resection, local Invasion, and tumor Size) scores < 6 were 77%, 82%, 84%, 86%, 85%, and 82%, respectively ($p = 0.06$). Lobectomy accounted for 70% of initial procedures during 1940–1949 and 22% during 1950–1959; during 1960–1999 bilateral lobar resection (BLR) accounted for 91% of surgeries ($p < 0.001$). RRA after BLR was performed during 1950–1969 in 3% but increased to 18%, 57%, and 46% in successive decades ($p < 0.001$). The 40-year rates for CSM and TR during 1940–1949 were significantly higher ($p = 0.002$) than during 1950–1999. During the last 50 years the 10-year CSM and TR rates for the 2286 cases did not significantly change with successive decades. Moreover, the 10-year rates for CSM and TR were not significantly improved during the last five decades of the study, either for the 1917 MACIS < 6 patients or the 369 MACIS ≥ 6 patients. Increasing use of RRA has not apparently improved the already excellent outcome, achieved before 1970, in low risk (MACIS < 6) PTC patients managed by near-total thyroidectomy and conservative nodal excision.

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy [1] and has accounted in recent years for about 80% of new cases of thyroid cancer seen in both the United States and Japan [2, 3]. Controversies about the surgical management of PTC were first addressed at the Mayo Clinic by Beahrs and Woolner [4] in 1959 and were not completely resolved during the next four decades [5, 6]. A principal reason for this lack of consensus has been the fact that there have never been any meaningful long-term prospective controlled therapeutic trials for this disease [1, 7]; consequently, all current treatment recommendations for patients with PTC have been based almost entirely on the basis of results derived from multivariate analysis of relatively uncontrolled retrospective studies [8]. This has not, however, prevented specialist societies of endocrinologists [9, 10], surgeons [11, 12], and oncologists [13] from producing during the past 5 years specific practice guidelines for the treatment of this increasingly recognized entity. The clear message from these recent recommendations is that in the twenty-first century most PTC patients in the United States will likely be considered eligible for an initial near-total or total thyroidectomy, almost routinely followed by "completion" of the thyroidectomy by postoperative administration of radioactive iodine (RAI) for remnant ablation [13–15]. It is not clear that such an aggressive approach is justifiable [1, 6, 7, 16].

At the Mayo Clinic (Rochester, Minnesota) there has been a long tradition of analyzing the results of surgical treatment for thyroid carcinoma. Balfour [17] in 1918 reported on 63 operable patients treated during 1910–1916, and 50 years later Woolner and his group [18] described long-term follow-up information on 1181 cases treated from 1926 to 1960. By 1986 McConahey et al. [19], describing a cohort of 859 PTC patients treated during 1946–1970, found that the overall mortality observed at 30 years was only 3% above that expected. Such excellent outcome data were accomplished despite the fact that only 16% underwent total thyroidectomy, and 97% did not have radioiodine remnant abla-

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tion (RRA). More recent analyses of Mayo Clinic patients treated since 1970 have raised serious doubts about the efficacy of RRA [1, 7], particularly in patients judged to be at low risk [6, 20] of either cause-specific mortality (CSM) or tumor recurrence (TR).

In terms of PTC management, the past six decades at the Mayo Clinic can be conveniently divided into four therapeutic eras, each of 15 years' duration [1, 7]. In the first (1940–1954), most PTC patients underwent unilateral lobectomy, a few had a near-total or total thyroidectomy, and almost none underwent RRA [4]. During the second era (1955–1969), most initially had near-total thyroidectomy, and fewer than 5% underwent ablation [19]. During 1970–1984 most PTC patients had near-total thyroidectomy or total thyroidectomy, and about one-third underwent ablation [7]. Since 1985, almost all PTC patients had an initial near-total or total thyroidectomy, and more than half underwent ablation. What is unclear is whether the increased aggressiveness of PTC management, especially seen in our practice since 1975, has translated into improved outcome in terms of long-term CSM and TR rates. The present study was devised in an attempt to clarify the changes in initial therapy for PTC patients at our institution during six decades from 1940 through 1999. Even more importantly, the study was aimed at determining whether the observed trend toward more aggressive therapy has led to significant improvements in patient outcome, especially the CSM and TR rates.

Methods

Patients and Follow-up

The records of all patients treated at the Mayo Clinic for PTC during 1940–1999 were reviewed. All relevant histologic slides were reexamined and reclassified according to the 1988 World Health Organization criteria [21] by an endocrine pathologist (J.R.G.) who had no knowledge of disease outcome. There were 2444 patients (1648 females, 796 males) who underwent definitive primary surgical therapy at the Mayo Clinic, had histologic reconfirmation of PTC, and were treated within 60 days of the initial diagnosis. Death certificates were examined for the 771 (32%) who were known to have died. Information regarding living patients was obtained by reexamination or by correspondence with the home physician, patient, or relatives [6, 7, 20]. There were 43,024 person-years of follow-up. The median follow-up was 15 years, and the longest follow-up was 60 years. Death was due to PTC in 106 (4%) cases. Excluded from the studies of tumor recurrence ($n = 129$, 5%) were those who had either distant metastasis discovered within 30 days of the initial surgery or had incomplete tumor resection, with gross residual disease persisting after resection.

Statistics

Comparisons of risk characteristics and trends across the decades were performed using chi-square tests of proportions or Fisher's exact test when necessary. Survival from the date of initial surgery to each endpoint (including CSM and TR) was analyzed using the Kaplan-Meier method [22]. The log-rank test was used to determine group differences in survival curves [23]. All tests were two-sided, with an alpha level of 0.05. All calculations were performed using SAS software [24].

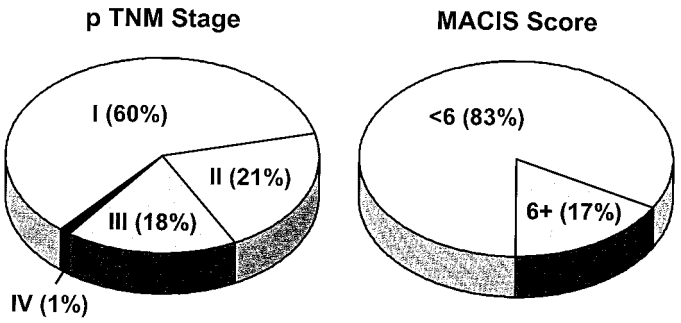

Fig. 1. Distributions of pTNM stages and MACIS (distant Metastasis, patient Age, Completeness of resection, local Invasion, and tumor Size) scores in 2444 consecutively treated patients with papillary thyroid carcinoma (PTC) managed at the Mayo Clinic during six decades (1940–1999).

Results

Patient and Tumor Characteristics

The median age of the patient at diagnosis of PTC was 46 years (range 4–90 years). The mean tumor size was 2.1 cm (median 1.7 cm; range 0.1–15.0 cm) in maximum diameter. The histologic grade [7, 19] was 1, 2, and 3 in 2327 (95%) 111, and 6 patients, respectively. DNA ploidy by flow cytometry [7] was diploid in 78%, tetraploid in 11%, and aneuploid in 11% of 470 cases studied. Tumors were demonstrated to be multicentric in 693 (28%) patients. Altogether, 328 (13%) of the primary tumors at presentation were locally invasive to extrathyroidal soft tissues, 983 (40%) had metastatic involvement of regional lymph nodes at the time of the initial surgery, and 45 (2%) had distant metastases found no later than 30 days after the date of the initial surgical procedure. Figure 1 illustrates the distributions of pTNM stages [25] and presenting MACIS (distant Metastasis, patient Age, Completeness of resection, local Invasion, and tumor Size) prognostic scores [26]. There were 1976 PTC patients (81%) who were either stage I or II at diagnosis, and 2038 (83%) had MACIS scores of < 6 (low risk). The median MACIS score was 4.43, and the range of scores was 3.15 to 15.34 (mean 4.81). During the six decades studied, the proportion of low risk PTC patients, with initial MACIS scores < 6 were 77%, 82%, 84%, 86%, 85%, and 82%, respectively ($p = 0.06$).

Initial Surgery and Postoperative RAI Administration

Bilateral lobar resection, performed in 2120 (86%), was the usual primary surgical procedure undertaken in PTC patients during the period of study. Overall, the most frequently performed primary surgical procedure was near-total thyroidectomy, which accounted for 1299 (53%) of the initial operations. Total thyroidectomy was the second most popular operation during the six decades studied and was performed in 606 cases (25%). Bilateral subtotal resection was performed in only 215 (9%). Unilateral thyroid lobectomy was the primary surgical procedure in 284 (12%); lesser procedures (including biopsy and subtotal lobectomy) were performed in the remaining 1% of patients. In only 107 (4%) cases was the tumor excision incomplete, where the surgeon reported the persistence of gross residual disease at the conclusion of the initial neck operation. There were 2305 patients (94%) who un-

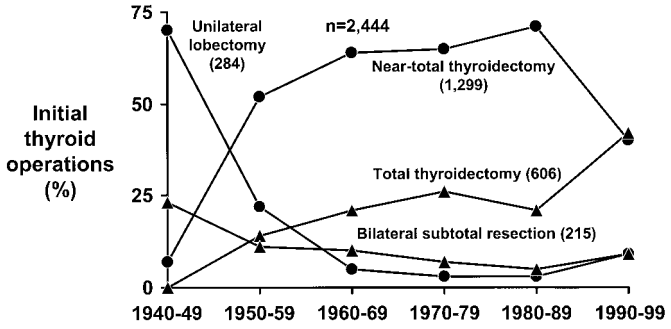

Fig. 2. Trends through six decades regarding the extent of initial surgical resection performed at the Mayo Clinic for the definitive therapy of PTC. Numbers in parentheses represent the numbers of patients undergoing that specific type of initial surgery during 1940–1999.

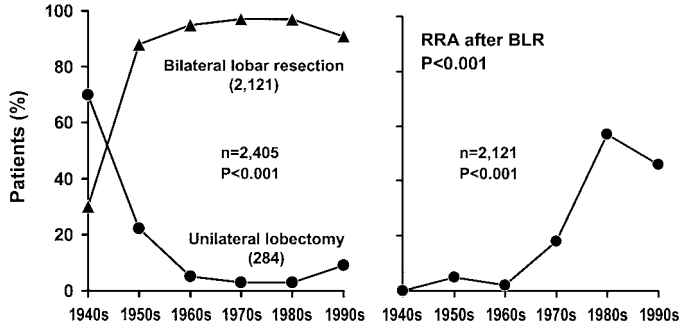

Fig. 3. Trends through six decades in the extent of initial surgery (**left**) and the proportion of patients having radioiodine remnant ablation (RRA) (**right**) after initial bilateral lobar resection (BLR) at the Mayo Clinic.

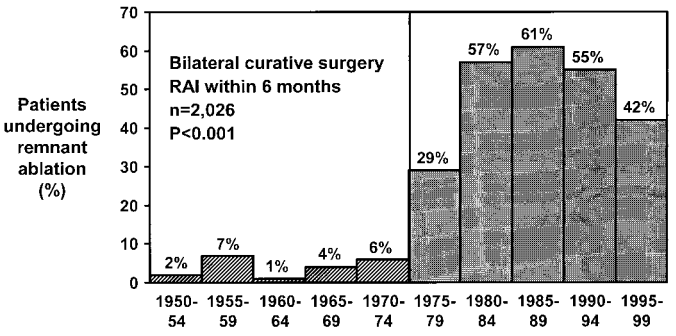

Fig. 4. Trend through five decades in RRA performed at the Mayo Clinic, within 6 months of potentially curative BLR, in 2026 PTC patients without initial distant metastases. RAI: radioactive iodine.

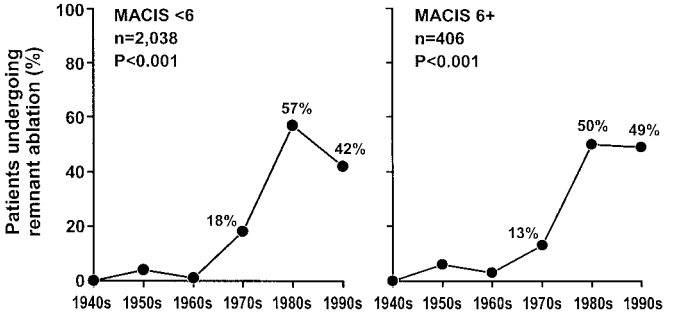

Fig. 5. Trends through six decades regarding the proportion of patients undergoing RRA, comparing 2038 low risk PTC patients with MACIS scores < 6 (**left**) with 406 high risk PTC patients with MACIS scores ≥ 6 (**right**).

derwent complete surgical resection, with no distant metastasis on initial examination or within 30 days of the primary operation. These potentially curable patients were considered eligible for postoperative RAI adjunctive therapy. At least 774 (33%) were given such therapy at some time after the primary operation, but only 637 (28%) underwent RRA within 6 months of initial surgery.

Trends in Extent of Surgical Resection during Six Decades

Figure 2 illustrates the significant changes ($p < 0.0001$) that occurred during the six decades of the study regarding the extent of the initial surgical resection performed at the Mayo Clinic for definitive therapy of PTC. During the first half of the study period, the proportion undergoing lobectomy fell from 70% during the 1940s, to 22% during the 1950s, to only 5% in the 1960s. During the 1940s only 7% had either near-total or total thyroidectomy, but this figure rose to 67% by the 1950s and to a peak of 92% by the 1980s. Overall, the most significant differences occurred in the relative proportions of patients having either lobectomy or bilateral lobar resection (BLR). As illustrated by Figure 3, these changes occurred mainly during the first 20 years of the study. During the 1940s only 30% underwent initial BLR, but this proportion rose to 78% by the 1950s and to 91% to 97% during 1960–1999.

Trends in Remnant Ablation after BLR during Six Decades

No PTC patient was treated with RRA at the Mayo Clinic during the 1940s; and during 1950–1969 only 22 (3%) of 651 patients treated by initial BLR underwent ablation (Fig. 3). During the subsequent three decades the comparable proportions undergoing RRA were 18%, 57%, and 46%, respectively. Figure 4 highlights the significant changes in the use of RRA in patients who had potentially curative BLR during 1950–1999 ($p < 0.001$). During 1970–1974 only 6% of 149 patients underwent RRA, but this increased dramatically to 29% of 205 patients treated during 1975–1979. The highest RRA rate (of 61%) was found during the period 1985–1989. For 1990–1994 this rate had fallen to 55%, and by 1995–1999 the comparable rate was further reduced to 42% of PTC patients undergoing BLR with complete surgical resection.

Figure 5 illustrates the proportions of low risk (MACIS scores < 6) and high risk (MACIS scores ≥ 6) PTC patients undergoing RRA during the six decades. During the 1970s and 1980s the use of RRA was not directed to the high risk cases. During the 1970s, 18% of low risk cases and only 13% of high risk cases were selected for RRA. Similarly, during the 1980s the proportion of ablated low risk cases again exceeded that seen with the MACIS ≥ 6 high risk group. It was only during the 1990s that proportionally more high risk cases were targeted for RRA; and during that

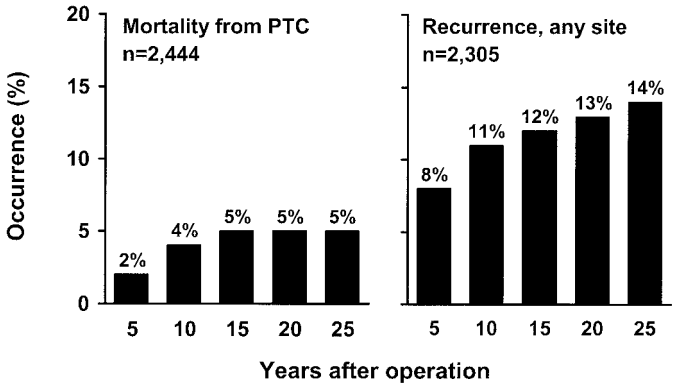

Fig. 6. Overall outcome of 2444 consecutively treated PTC patients managed at the Mayo Clinic during six decades (1940–1999), demonstrating 5- to 25-year rates for cause-specific mortality (**left**) and tumor recurrence at any anatomic site (**right**).

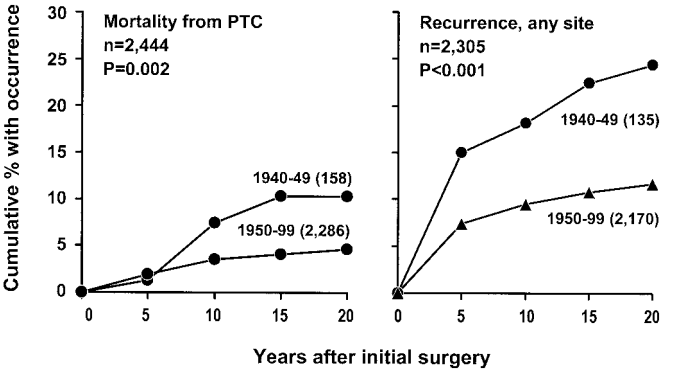

Fig. 8. Comparison of cumulative occurrence rates for cause-specific mortality (**left**) and tumor recurrence at any site (**right**) between PTC patients treated at the Mayo Clinic during the 1940s and those treated during the subsequent five decades (1950–1999).

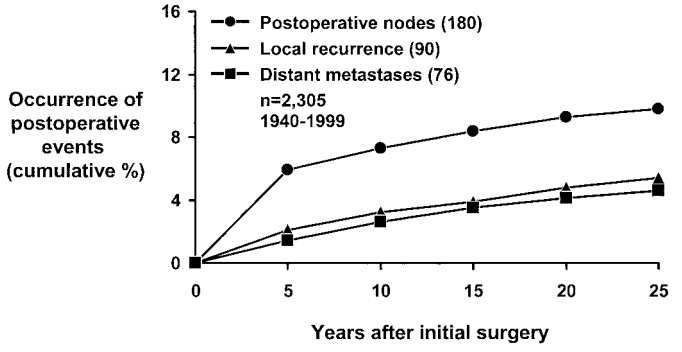

Fig. 7. Cumulative occurrence during 25 years of postoperative events: metastatic nodes (180 patients), local recurrences (90 patients), or distant metastases (76 patients). Data are from 2305 PTC patients with disease confined to the neck who initially underwent complete tumor resection at the Mayo Clinic during six decades (1940–1999).

period the percentage of low risk cases undergoing RRA fell from 57% during the 1980s to 42% during 1990–1999.

Overall Postoperative Outcome

To date, 771 (32%) of the 2444 patients have died, and 106 (4%) died directly from PTC. For a comparable population living in the north central United States during this period, the expected number of deaths from all causes would have been 700, a difference that is highly significant ($p = 0.006$). If one considers the survival to death from all causes in the potentially surgically cured group of 2305 (having complete surgical resection and presenting with disease localized to the neck), the observed number of deaths was 673, insignificantly different ($p = 0.949$) from the total expected of 671.

Figure 6 illustrates the CSM and TR rates observed over 25 postoperative years in the total group of 2444 patients. CSM rates were 5% at 15, 20, and 25 years. The TR rates were 8% at 5 years and 11% at 10 postoperative years for the subgroup of 2305 who had localized disease that was completely excised at the initial surgery. By 25 years the TR rate was as high as 14%. Figure 7 demonstrates that the most frequent site of TR was the regional (neck) lymph nodes, accounting to date for almost 60% of the total number of postoperative events. At 25 postoperative years, the recurrence rates at regional, local, and distant sites were 9%, 5%, and 4%, respectively.

Trends in Mortality and Recurrence Rates during Six Decades

The CSM rate at 10 postoperative years was significantly higher ($p = 0.002$) for the 158 patients treated during 1940–1949 when compared to the rates for the 2286 patients treated during 1950–1999 (Fig. 8, left panel). At 10 postoperative years the CSM rate for the 1940–1949 cohort was 7.4% compared to the rates of 4.3%, 5.6%, 3.0%, 2.2%, and 2.3% seen in successive decades ($p = 0.021$). At 40 postoperative years the CSM rate for the 1940–1949 cohort was 14% compared to 6% in those treated during 1950–1999 ($p = 0.0022$). There was no significant improvement in CSM rates during the five successive decades of the 1950–1999 time period ($p = 0.353$). Similarly significant differences ($p < 0.001$) were seen for TR between the 1940–1949 and 1950–1999 cohorts of treated patients (Fig. 8, right panel). At 10 postoperative years the TR rate for the 1940–1949 cohort was 18.2% compared to rates of 9.3%, 7.7%, 9.7%, 8.2%, and 10.4% seen during successive decades ($p < 0.0001$). At 40 postoperative years the TR rate for the 1940–1949 cohort was 32% compared to 13% in the 1950–1999 cohort ($p < 0.001$). There was no significant improvement in TR rates during the five successive decades of the 1950–1999 time period ($p = 0.062$).

Outcome Trends for High Risk and Low Risk PTC during 1950–1999

Because of the significantly worse outcome seen for both CSM and TR in the 1940–1949 cohort, the final analyses of outcome trends were confined to the 1950–1999 cohort of 2286 patients, of whom 1917 (84%) had MACIS scores < 6. Figure 9 illustrates the changes in CSM and TR during successive decades in the 369 high risk PTC patients with MACIS scores of ≥ 6. Although there appears to be a downward trend in the 10-year CSM rates, the trend was not significant ($p = 0.45$); and during the 1990s the rate at 10 years was 12.4%. Similarly, there appeared to be no significant improvement ($p = 0.98$) in the TR rates between the 1960s

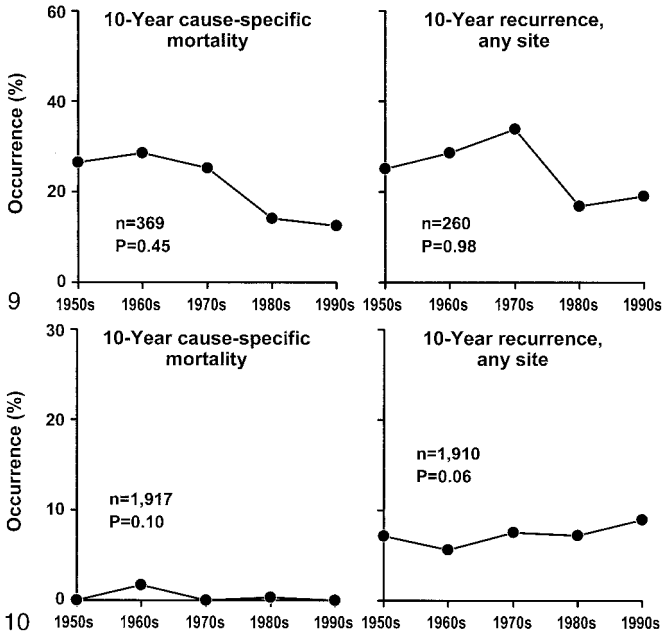

Fig. 9. Trends through five decades in 10-year rates for cause-specific mortality (**left**) and tumor recurrence at any site (**right**) for 369 high risk PTC patients (MACIS score ≥ 6) who had their primary treatment at the Mayo Clinic during 1950–1999.

Fig. 10. Trends through five decades in 10-year rates for cause-specific mortality (**left**) and tumor recurrence at any site (**right**) for 1917 low risk PTC patients (MACIS scores < 6) who had their primary treatment at the Mayo Clinic during 1950–1999.

and the 1990s, with the most recent rate at 10 years being 19%. Figure 10 demonstrates comparable data for the 1917 patients with MACIS scores < 6. It is of interest that the cause-specific survival at 10 years is 100% for the 534 low risk cases treated during the 1990s, at a time when more extensive BLR was usual, and many underwent ablation. However, it should be recognized that the survival was also 100% for the 332 patients treated during the 1970s, when ablation was performed in only a small number of patients. Even more remarkably, the 318 patients treated during the 1950s, when RRA was being employed in only a fraction of cases, also enjoyed a 100% cause-specific survival. Not surprisingly, there is no significant change ($p = 0.64$) in the CSM rates during the five decades of 1950–1999. With regard to the 10-year TR rates, there is certainly no evidence of a significant downward trend in the rates during successive decades. Indeed, the trend upward from 7.1% in the 1950s through 7.4% in the 1970s to the most recent figure of 8.8% in the 1990s almost reaches significance ($p = 0.06$). This upward trend in TR rate during the last decade likely reflects the increasing sensitivity of locoregional recurrence detection using immunometric assays of serum thyroglobulin (Tg), and the more frequent use of fine-needle aspiration (FNA) biopsies guided by high-resolution ultrasonography (HRUS) of the neck postoperatively [27]. Overall, despite increased use of RRA since 1975, there has been no significant improvement in outcome (as evidenced by CSM and TR rates) in either the 369 high risk or the 1917 low risk PTC cases treated at the Mayo Clinic during the last five decades.

Discussion

Careful analysis of the therapeutic trends at the Mayo Clinic during the six decades from 1940 through 1999 suggests that the two most important practice changes observed during that period were the introduction during the 1950s of near-total and total thyroidectomy and, during 1970–1989 the increasing use of postoperative RRA. During the 1970s and 1980s RRA was more often used in low risk (MACIS < 6) cases, although by the 1990s slightly more of the high risk (MACIS ≥ 6) PTC patients were now receiving ablative RAI doses within 6 months of initial surgery.

During those same six decades there were meaningful advances in the sophistication of the techniques employed for the surveillance of patients operated on for PTC. The 1980s saw the introduction of ever more sensitive immunometric assays for serum thyroid-stimulating hormone (TSH) and Tg, as well as increasing use of computed tomography (CT) and magnetic resonance imaging (MRI) of the neck postoperatively by the diagnostic radiologist. The late 1980s saw the advent of HRUS of the neck, associated with the opportunity of performing guided biopsies of thyroid bed recurrent nodules or suspicious cervical lymphadenopathy [27]. More recently, during the late 1990s, positron emission tomography has been introduced to the evaluation of the postoperative neck [28] and recombinant human TSH (rhTSH) has become available to enable patients to undergo whole body scanning with RAI without the inconvenience of thyroid hormone withdrawal [29]. Indeed, one might have the impression from recent literature that the criterion for "cure" of PTC during the present era may require demonstration of an undetectable serum Tg on thyroxine suppressive therapy that will not be significantly stimulated by either rhTSH or hormone withdrawal [12, 13, 15, 29].

Since 1950 the prognosis for PTC surgically treated at the Mayo Clinic has been excellent, with 40-year CSM and TR rates being only 6% and 13%, respectively. When outcome during each of the six decades was studied, it was apparent that the only significant improvement occurred between the first and second decades. During that period the 20-year CSM rate fell from 10% to 5% and the TR rate from 24% to 12%. By contrast, despite increasing use of RRA since 1975, there was not, during the last two decades (1980–1999), any further demonstrable improvement in outcome (CSM or TR) in the high risk cases (MACIS scores ≥ 6) or the low risk cases (MACIS scores < 6). This is an extraordinary finding when one considers the apparent advances that have occurred in clinical chemistry and diagnostic radiology, as outlined above.

From the present results, one might conclude that the more widespread use of RRA has not been associated with a significant improvement in the already excellent CSM and TR rates found in PTC patients with MACIS scores < 6. In such low risk PTC patients, an initial management program consisting of BLR (usually near-total thyroidectomy), conservative neck nodal excision, and postoperative levothyroxine suppression appears to be justified.

In 1994 DeGroot [30] summarized the status of RRA as follows:

"Mazzaferri, Young and coworkers provided, nearly two decades ago, the first powerful support for the role of radioiodine treatment in reducing recurrences and deaths in differentiated [thyroid] cancer . . . more recent studies by DeGroot and col-

leagues, and Samaan and coworkers demonstrated, in a careful analysis, stratifying patients by extent of diseases, that both more extensive surgery (lobectomy plus subtotal or near-total thyroidectomy) and radioactive iodine treatment reduce the number of recurrences and deaths. Hay and coworkers have thrown their support behind more extensive surgery, but have not yet supported routine radioactive iodide ablation."

It is still our stance that routine RRA in all PTC patients is unjustifiable; and in our opinion the outcome results, described in this report, should raise serious doubts about the efficacy of RRA in eliminating tumor recurrence in patients with low risk (MACIS < 6) PTC. For that reason the Division of Endocrinology at the Mayo Clinic has, since 1994, stopped recommending RRA to patients with low risk PTC. On the other hand, RRA is still being advised for the postoperative management of those few patients who are (with initial MACIS scores of ≥ 6), at significantly increased risk of both tumor recurrence and death from papillary cancer. In our opinion, we are moving much closer to providing satisfactory answers to Sisson's comments [31], who in 1983 suggested that for the treatment of PTC, "each physician who treats thyroid cancer must decide from incomplete knowledge whether to use ^{131}I as a radioactive eraser. To ablate or not to ablate is a question that will haunt us for some time to come." It is our earnest hope that, for patients with low risk (MACIS < 6) PTC, the era of the "radioactive eraser" will soon be a memory from the last quarter of the twentieth century.

Résumé. On ignore si la chirurgie primitive étendue associée à la radioablation (RA) améliore la mortalité spécifique (MS) ou le taux de récidive tumorale (RT) des carcinomes papillaires de la thyroïde (CPT). Grâce à l'information contenue dans une banque de données informatisée, on présente ici les détails de la présentation initiale, la thérapeutique et l'évolution chez 2444 patients porteurs d'un CPT, traités de façon consécutive pendant les années 1940–1999. Les patients ont été suivis plus de 43000 patient-années. La MS et le taux de RT à 25 ans ont été, respectivement, de 5% et de 14%. On a analysé les tendances avec le temps pendant les six décennies: la proportion de patients ayant un score initial «MACIS» inférieur à 6 ont été, respectivement, de 77%, 82%, 84%, 86%, 85%, et 82% ($p = 0.06$). Pendant la période 1940–49, 70% des procédés initiaux ont été des lobectomies; ce chiffre est descendu à 22% pour la période 1950–59. Pendant la période 1960–1999, on a effectué une lobectomie bilatérale (LBL) chez 91% des patients ($p < 0.001$). Une RA après LBL a été réalisée pendant la période 1950–1969 chez 3%, mais a ensuite augmenté à 18%, à 57% et à 46% dans les décennies suivantes successives ($p < 0.001$). Les taux de MS et de RT à 40-ans ont été significativement plus élevés ($p = 0.002$) pendant la période 1940–1949 que pendant la période 1950–1999. Au cours des cinq décennies successives les taux de MS et de RT (2286 cas) n'ont pas changé de façon significative. De plus, les taux de MS et de RA à 10 ans ne se sont pas améliorés pendant les cinq dernières décennies de l'étude, que ce soit pour les 1917 patients MACIS < 6 ou pour les 369 patients MACIS 6 ou +. Une augmentation de la RA n'a pas apparemment amélioré l'évolution déjà excellente, réalisée avant 1970, chez les patients CPT à bas risque (MACIS < 6), traités par thyroïdectomie presque totale et une lymphadénectomie conservatrice.

Resumen. Se desconoce si la cirugía inicial ampliada y una indicación más liberal en el tratamiento con radioyodo (RRA) podría mejorar la mortalidad relacionada con el tumor (CSM) o disminuir las recidivas (TR) en el cáncer papilar de tiroides (PTC). En un banco de datos computarizado se han recogido los detalles del inicio de la enfermedad, tratamiento y resultados obtenidos en 2444 pacientes con PTC, tratados entre 1940 y 1999. Se efectuó un seguimiento a más de 43,000 pacientes por año y los porcentajes a los 25 años para la CSM y TR fueron del 5 y 14%. La tendencia temporal se analizó para cada una de las 6 décadas. Durante las 6 décadas la proporción inicial con la valoración de MACIS < 6 fue del 77%, 82%, 84%, 86%, 85% y 82% ($p = 0.06$). Entre 1940–1949 el tratamiento inicial, en el 70% de los casos, fue la lobectomía tiroidea cuya frecuencia entre los años 1950–59 sólo fue del 22%. De 1960 a 1999 se practicó en el 91% de los casos ($p < 0.001$) una resección bilobar (BLR), RRA tras BLR se indicó entre 1950–1969 en el 3% de los pacientes, incrementándose en las décadas sucesivas al 18%, 57%, y 46% ($p < 0.001$). A los 40 años el porcentaje de CSM y TR durante el periodo 1940–1949 fue significativamente mayor ($p = 0.002$) que durante el periodo comprendido entre 1950–1999. En los últimos 50 años el porcentaje del CSM y TR a los 10 años, para 2286 casos estudiados, no se modificó significativamente con relación a las diversas décadas. Es más, los porcentajes de CSM y TR a los 10 años, no mejoró en las 5 últimas décadas del estudio, tanto para los 1917 pacientes con un MACIS < 6, como para los 369 pacientes con un MACIS superior a 6. Por tanto, el mayor empleo del radioyodo en el tratamiento del remanente tiroideo tras la ablación quirúrgica, no consiguió mejorar los excelentes resultados obtenidos antes de 1970, en pacientes con PTC de bajo riesgo (MACIS < 6) tratados con tiroidectomía subtotal y vaciamiento ganglionar conservador.

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