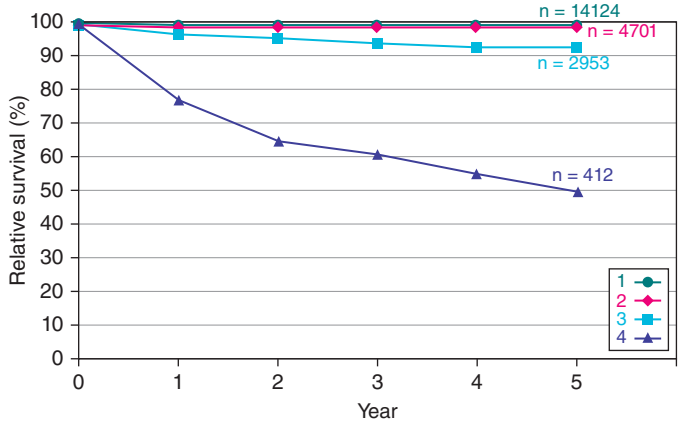

FIGURE 405-12 Survival rates of patients with different stages of papillary cancer. *(Adapted with permission from Edge SB, Byrd DR: Thyroid, in Compton CC, Fritz AB, Greene FL, Trotti A [eds]: AJCC Cancer Staging Manual, 7th ed. New York, Springer, 2010, pp 87–92.)*

TREATMENT WELL-DIFFERENTIATED THYROID CANCER

SURGERY

All well-differentiated thyroid cancers should be surgically excised. In addition to removing the primary lesion, surgery allows accurate histologic diagnosis and staging, and multicentric disease is commonly found in the contralateral thyroid lobe. Preoperative sonography should be performed in all patients to assess the central and lateral cervical lymph node compartments for suspicious adenopathy, which if present, can undergo FNA and then be removed at surgery. Bilateral, near-total thyroidectomy has been shown to reduce recurrence rates in all patients except those with T1a tumors (≤1 cm). If cytology is diagnostic for thyroid cancer, bilateral surgery should be done. If malignancy is identified pathologically after lobectomy, completion surgery is recommended unless the tumor is T1a or is a minimally invasive follicular cancer. Bilateral surgery for patients at higher risk allows monitoring of serum Tg levels and administration of radioiodine for remnant ablation and potential treatment of iodine-avid metastases, if indicated. Therefore, near-total thyroidectomy is preferable in almost all patients; complication rates are acceptably low if the surgeon is highly experienced in the procedure.

TSH SUPPRESSION THERAPY

Because most tumors are still TSH-responsive, levothyroxine suppression of TSH is a mainstay of thyroid cancer treatment. Although TSH suppression clearly provides therapeutic benefit, there are no prospective studies that define the optimal level of TSH suppression. The degree of TSH suppression should be individualized based on a patient's risk of recurrence. It should be adjusted over time as surveillance blood tests and imaging confirm absence of disease or, alternatively, indicate possible residual/recurrent cancer. For patients at low risk of recurrence, TSH should be suppressed into the low but detectable range (0.1–0.5 mIU/L). If subsequent surveillance testing indicates no evidence of disease, the TSH target may rise to the lower half of the normal range. For patients at high risk of recurrence or with known metastatic disease, TSH levels should be kept to <0.1 mIU/L if there are no strong contraindications to mild thyrotoxicosis. In this instance, unbound T_4 must also be monitored to avoid excessive treatment.

RADIOIODINE TREATMENT

After near-total thyroidectomy, substantial thyroid tissue often remains, particularly in the thyroid bed and surrounding the parathyroid glands. Postsurgical radioablation of the remnant thyroid eliminates residual normal thyroid, facilitating the use of Tg determinations and radioiodine scanning for long-term follow-up. In addition, well-differentiated thyroid cancer often incorporates radioiodine, although less efficiently than normal thyroid follicular cells. Radioiodine uptake is determined primarily by expression of the NIS and is stimulated by TSH, requiring expression of the TSH-R. The retention time for radioactivity is influenced by the extent to which the tumor retains differentiated functions such as iodide trapping and organification. Consequently, for patients at risk of recurrence and for those with known distant metastatic disease, ^{131}I ablation may also potentially treat residual tumor cells.

Indications Not all patients benefit from radioiodine therapy. Neither recurrence nor survival rates are improved in stage I patients with T1 tumors (≤2 cm) confined to the thyroid. However, in higher risk patients (larger tumors, more aggressive variants of papillary cancer, tumor vascular invasion, presence of large-volume lymph node metastases), radioiodine reduces recurrence and may increase survival.

^{131}I Thyroid Ablation and Treatment As noted above, the decision to use ^{131}I for thyroid ablation should be coordinated with the surgical approach, because radioablation is much more effective when there is minimal remaining normal thyroid tissue. Radioiodine is administered after iodine depletion (patient follows a low-iodine diet for 1≤2 weeks) and in the presence of elevated serum TSH levels to stimulate uptake of the isotope into both the remnant and potentially any residual tumor. To achieve high serum TSH levels, there are two approaches. A patient may be withdrawn from thyroid hormone so that endogenous TSH is secreted and, ideally, the serum TSH level is >25 mIU/L at the time of ^{131}I therapy. A typical strategy is to treat the patient for several weeks postoperatively with liothyronine (25 μg qd or bid), followed by thyroid hormone withdrawal for 2 weeks. Alternatively, recombinant human TSH (rhTSH) is administered as two daily consecutive injections (0.9 mg) with administration of ^{131}I 24 h after the second injection. The patient can continue to take levothyroxine and remains euthyroid. Both approaches have equal success in achieving remnant ablation.

A pretreatment scanning dose of ^{131}I (usually 111–185 MBq [3–5 mCi]) or ^{123}I (74 MBq [2 mCi]) can reveal the amount of residual tissue and provides guidance about the dose needed to accomplish ablation. However, because of concerns about radioactive "stunning" that impairs subsequent treatment, there is a trend to avoid pretreatment scanning with ^{131}I and use either ^{123}I or proceed directly to ablation, unless there is suspicion that the amount of residual tissue will alter therapy or that there is distant metastatic disease. In the United States, outpatient doses of up to 6475 MBq (175 mCi) can be given at most centers. The administered dose depends on the indication for therapy with lower doses of 1850–2775 MBq (50–75 mCi) given for remnant ablation but higher doses of 3700–5500 MBq (100–150 mCi) used as adjuvant therapy when residual disease may be present. A WBS following radioiodine treatment is used to confirm the ^{131}I uptake in the remnant and to identify possible metastatic disease.

Follow-Up Whole-Body Thyroid Scanning and Thyroglobulin Determinations Serum thyroglobulin is a sensitive marker of residual/recurrent thyroid cancer after ablation of the residual postsurgical thyroid tissue. However, newer Tg assays have functional sensitivities as low as 0.1 ng/mL, as opposed to older assays with functional sensitivities of 1 ng/mL, reducing the number of patients with truly undetectable serum Tg levels. Because the vast majority of papillary thyroid cancer recurrences are in cervical lymph nodes, a neck ultrasound should be performed about 6 months after thyroid ablation; ultrasound has been shown to be more sensitive than WBS in this scenario.

In low-risk patients who have no clinical evidence of residual disease after ablation and a basal Tg <1 ng/mL on levothyroxine, an rhTSH-stimulated Tg level should be obtained 6–12 months after ablation, without WBS. If stimulated Tg levels are low (<1 ng/mL)