Controversy Over Radioiodine Ablation In Thyroid Cancer: Who Benefits?

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KEYWORDS

• Thyroid cancer • Radioiodine ablation • RIA • Risk stratification • Overdiagnosis

KEY POINTS

- Since the early 1970s, the incidence of thyroid cancer, mainly papillary, in the United States has almost tripled with unchanged mortality.
- The extent of surgery performed for small thyroid cancers is controversial but only patients who have undergone total thyroidectomy are candidates for radioiodine ablation (RIA).
- RIA in low-risk patients has not been shown to decrease mortality and may not be indicated.
- Intermediate-risk patients may benefit from selective administration of RIA.
- Retrospective data support the use of iodine-131 (I-131) in high-risk patients, resulting in decreased recurrence and improved mortality.
- Lower doses of I-131 have been proven effective for RIA of remnant thyroid tissue after thyroidectomy.

INTRODUCTION

In the United States, the first use of radioactive iodine therapy as an alternative to surgery for toxic goiter was in 1943. Its subsequent use in the treatment of thyroid cancer was documented in 1948 in a patient with hyperthyroidism due to pulmonary metastases.[1] In the 1950s and 1960s, the ability of neoplastic thyroid tissue to concentrate radioactive iodine and cause subsequent destruction was elucidated. Soon there were reports of improved survival in patients suffering with metastatic thyroid cancer who were treated with radioiodine ablation (RIA).[2] Over the last 70 years, the use of RIA in well-differentiated thyroid cancer has evolved and become the standard of care in many cases. The concept of thyroid remnant ablation was introduced in the 1970s[3]

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Surg Clin N Am 94 (2014) 573–586
http://dx.doi.org/10.1016/j.suc.2014.03.004 **surgical.theclinics.com**
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and, in an effort to eradicate thyroglobulin production, is now cited as one of the main goals of therapy.[4]

Currently, about 50% of patients diagnosed with thyroid cancer will receive adjuvant RIA.[5] However, there is still considerable controversy about the appropriate role of RIA in thyroid cancer. In the United States, recommendations for appropriate use of RIA come from the organizations American Thyroid Association (ATA) and National Comprehensive Cancer Network (NCCN), with consensus guidelines predominantly based on retrospective cohort studies.[4,6] Until recently, large prospective randomized studies evaluating the use of RIA had not been published. The controversy concerning RIA is complicated by the ever-increasing numbers of small, low-risk thyroid cancers being diagnosed. To better understand some of the controversies, the evolving epidemiology of the disease must be examined.

EPIDEMIOLOGY

The incidence of thyroid cancer in the United States has almost tripled since the early 1970s and nearly doubled during the last decade, especially in women. Thyroid cancer is now the fifth most common cancer in women in the United States.[7] Despite this continued increase in incidence, the mortality rate from thyroid cancer has not significantly changed.[7] The 2013 US statistics for thyroid cancer estimate 60,220 new cases (45,310 women and 14,910 men). However, the number of deaths estimated are only 1850 (1040 women and 810 men).[8]

The reasons for such a steep increase in thyroid cancer incidence were not well understood until recently. The study by Chen and colleagues[9] investigated the increasing incidence of differentiated thyroid cancer in the United States from 1988 to 2005 and found the highest rate of increase was for small, localized thyroid cancers. It suggested that the increase was partly due to better cancer detection by ultrasonography and other imaging techniques. They also found an increased incidence across all tumor sizes and suggested that increased diagnostic scrutiny is not the sole explanation. Other possible causes, including environmental influences, should be considered.

Another study by Nikiforov[10] hypothesized that increased exposure to ionizing radiation, a known risk factor, especially for papillary thyroid cancer (PTC), may be playing a role. Historically, increased incidence of papillary thyroid carcinomas have occurred in areas of high radiation exposure. Specific examples include children in the Marshall Islands after atomic bomb testing and in the Ukraine after the Chernobyl nuclear accident.[11,12]

However, ionizing radiation is an unlikely explanation for the marked increase in incidence of thyroid cancer in the United States,[13] where the highest amount of radiation is from background exposure to radon, followed by medical radiation, including CT scans.[13,14] Although there has been increasing attention paid to rising levels of medical radiation, the attributable cancer risk from medical imaging is relatively low and certainly would not be expected to account for a significant component of the rising thyroid cancer incidence.

Another explanation for the explosion of thyroid cancer diagnoses is increased detection during pathologic evaluation of surgical specimens. In a 40-year retrospective study of 2260 thyroidectomies for retrosternal goiter without known history of thyroid cancer, Grodski and colleagues[15] showed that the percentage of thyroid cancer increased from 3.6% to 7.5% over time ($P<.05$). However, once papillary thyroid microcarcinomas (PTMCs), which are defined as small PTCs less than 1 cm by the World Health Organization,[16] were excluded, there was no increase in cancer

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