HHS Public Access

Author manuscript

Curr Opin Endocrinol Diabetes Obes. Author manuscript; available in PMC 2018 October 01.

Published in final edited form as:

Curr Opin Endocrinol Diabetes Obes. 2017 October ; 24(5): 332–336. doi:10.1097/MED.0000000000000359.

The Thyroid Cancer Epidemic, 2017 Perspective

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Abstract

Purpose of review—Thyroid cancer incidence and mortality trends have been identified as being consistent with overdiagnosis, and several recent efforts have been made to mitigate this problem.

Recent findings—Major guidelines for thyroid nodule management recommend against general biopsy of nodules <1 cm in size. Data supporting the safety of active surveillance of low risk thyroid cancers is now recognized. Tumors previously labeled as encapsulated follicular variant papillary thyroid cancers are now recommended to be called non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

Summary—Workup, diagnostic, and management of papillary thyroid cancer are changing rapidly to accommodate the recognition that many thyroid cancers are low risk and do not require aggressive, immediate intervention

Keywords

thyroid neoplasm; incidence; thyroid nodules; overdiagnosis; cost effectiveness

Introduction

Since the 1990s, thyroid cancer incidence has been increasing faster than any other cancer type in the United States. This has been referred to as an epidemic of overdiagnosis because of the prevalence of low risk, non-lethal tumors that are often incidentally detected from a large subclinical reservoir of disease.[1–3] The most recent epidemiologic data, as well as several recent developments in recommendations about the diagnosis and management of low risk thyroid cancer, provide hope that the epidemic may be beginning to slow. Here we review recent incidence and mortality data, and discuss new discussions about trends in the

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Conflicts of interest: Dr. Morris reports that he has been a speaker for Pfizer.

United States. Then, we review new guidelines for thyroid cancer and other efforts to reduce the overdiagnosis and overtreatment of low risk thyroid cancer.

Current trends in thyroid cancer incidence and mortality

There are projected to be 56,780 new cases of thyroid cancer in the United States in 2017. Thyroid cancer remains one of the least deadly human cancers. In the U.S. there will be an estimated 2,010 deaths from thyroid cancer in 2017, whereas lung cancer, for example, will cause more than 155,000 deaths[4]. Thyroid cancer incidence prior to the mid 1990s was relatively stable, around 5/100,000. The incidence then increased to 15.0 in 2014, the last year of available data. Women have seen the highest increase in incidence, with 22.2 new cases per 100,000 people diagnosed in 2014. The rise in incidence has been due almost entirely to the most common histologic type, papillary thyroid cancer[5].

International incidence trends

Increased incidence of thyroid cancer with attribution to overdiagnosis has also been described outside of the United States. Using observed versus expected data from the Cancer Incidence in Five Continents, International Agency for Research on Cancer estimates, the incidence of thyroid cancer in South Korean women aged 50–59 in the years 2003–2007 was 120 cases per 100,000[6] (as compared to 22.2 in the United States in 2014). Similar large increases in incidence were seen in other developed nations where patients have high access to healthcare, the main driver of increased detection. The study estimated the rate of overdiagnosis, concluding that among women in the United States between 1998 and 2007, 228,000 cases of thyroid cancer, representing between 70–80% of cases, were asymptomatic lesions that would have gone undetected during a patient's lifetime if ultrasound and other imaging studies were not available. Similarly, 90% of cases in South Korea, 70–80% of cases in Italy, France, and Australia, and 50% of cases in Japan, the Nordic countries, and England and Scotland likely represented overdiagnosis among women during that time period.

Plateauing in Incidence

Recent data suggests that the rising incidence and overdiagnosis of thyroid cancer may be starting to slow. A study using SEER data described an annual percent change (APC) in thyroid cancer incidence in the United States of approximately 8% between 2000 and 2009, dropping to 2.8% annually in women and 3% annually in men during 2009–2012[7]. While this is an early trend, it may mark the beginning of meaningful changes in the detection of low risk thyroid cancer. A stable incidence would not represent a reversal of the rate of overdiagnosis, but it would at least suggest that the phenomenon is not getting worse. In South Korea, where the increased incidence was most dramatic, as public awareness increased, surgery rates spontaneously dropped[8]

Mortality Trends

A recent paper using SEER data described the incidence-based mortality from thyroid cancer of all histologies increased in the United States from an average of 0.40 per 100,000 person-years during 1994–1997, to an average of 0.46 per 100,000 person-years during

2010–2013. This represented an average relative annual increase in mortality of 1.1% per year. The overall rate of change in mortality was not significant for those with papillary cancers except among patients with advanced stage papillary thyroid cancers at the time of presentation. The authors concluded from this study that in addition to an increase in incidence due to overdiagnosis, there is potentially also a true increase in papillary thyroid cancer incidence, which they hypothesized may be due to environmental factors[9]. Reaching conclusions about whether this very small change in mortality rate means there are new causes of thyroid cancer is not yet possible. For example, during the 1980's to 1990's, when prostate cancer screening was common, and thus observed incidence rose, mortality due to prostate cancer also rose. When prostate cancer detection rates came back down after screening became less common, mortality also fell. The rise and fall in prostate cancer could also be what we are observing in thyroid cancer: attribution bias[10]. Attribution bias is when the cause of death in a patient's medical record is incorrectly labeled as due to the cancer, when in fact it was due to other causes.

Efforts to decrease overdiagnosis and overtreatment of thyroid cancer

Since about 2015, there have been a variety of efforts to mitigate the role of overdiagnosis in the increasing incidence of thyroid cancer. They have ranged from public education efforts to guideline and diagnostic changes.

No biopsy of thyroid nodules <1cm endorsed in ATA 2015 Guidelines

The American Thyroid Association (ATA) released guidelines in 2015 recommending a risk-stratified approach to utilizing fine needle aspiration (FNA) biopsy of thyroid nodules, in which nodules <1cm in size should generally not be biopsied. The text, but not the summary guideline statement, makes a few exceptions for patients with high-risk clinical factors or the presence of suspicious lymph nodes.[11] To date, there is no evidence regarding the impact of this recommendation, but if there is uptake of the guidelines, it should lead to a reduction in the cytologic diagnosis of papillary microcarcinoma (PMC; tumor <1cm), a low-risk thyroid cancer.

Active surveillance acknowledged in ATA 2015 Guidelines

As significant, if not more so, than the recommendation regarding biopsy of thyroid nodules, the ATA 2015 guidelines for the first time recognized active surveillance as a potential management approach for patients with low risk thyroid cancer. This includes patients with very low risk tumors (e.g. papillary microcarcinomas), patients at high surgical risk because of comorbidities, patients with an expected short remaining life span, or patients with concurrent medical or surgical issues that are more pressing than thyroid surgery.

The data supporting an active surveillance approach come from two Japanese cohorts, in which there were no deaths related to thyroid cancer in patients who did not have surgery.[12,13] Around 10% of followed patients eventually underwent surgery for various reasons, including patients who showed tumor enlargement on serial ultrasounds. Early data from the U.S. experience have been presented, with similar results so far[14].

Reclassification of some thyroid cancers to Non-Invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP)

In 2016, an international group of thyroid pathologists, endocrinologists and surgeons, acting on the imperative to reclassify indolent tumors as benign when appropriate, recommended a change to the nomenclature of a subset of thyroid lesions, removing the word “cancer” from the description. Prior to this group’s work, these tumors were called encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC). This group reviewed 109 cases of this entity and found that, compared to cases where the tumor was not encapsulated, there were no recurrences, metastases, or deaths from disease. They therefore recommended that the entity be renamed noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), which they hypothesized would “affect a large population of patients worldwide and result in a significant reduction in psychological and clinical consequences associated with the diagnosis of cancer.”[15]

USPSTF recommends against thyroid cancer screening

In 2017 the United States Preventative Services Taskforce (USPSTF) gave thyroid cancer screening in asymptomatic individuals a grade of “D,” which means a recommendation against screening.[16] This review of the more recent literature was consistent with prior reviews. The Task Force concluded with moderate or high certainty that screening in people without symptoms has no net benefit or that the harms outweigh the benefits. Clinicians are therefore recommended not to screen for thyroid cancer either with ultrasound, neck palpation, or other modalities in patients without symptoms. Since most thyroid cancers that would be found by screening would be low risk subclinical disease, finding these cancers would be unlikely to change mortality rates, and would lead to potential harms from treatment. The few patients who have aggressive thyroid cancers that cause mortality almost uniformly present with symptoms; screening in the large asymptomatic population would be unlikely to detect these few cases or change the trajectory of their outcomes.[17]

Media exposure of thyroid cancer overdiagnosis has affected patient and physician behavior

In South Korea, rates of thyroid cancer detection sky rocketed due to screening with thyroid ultrasound.[18] A group of physicians in South Korea made a high-profile public appeal in print and on television recommending against thyroid screening with ultrasound. The result was a 35% reduction in the number of thyroidectomies performed in the subsequent year. This seems to be a striking example that the issue of overdiagnosis and overtreatment resonates with patients, and that public awareness can lead to changes in behavior.[8]

Modeling of thyroid cancer care costs by management strategy

The cost of thyroid cancer care in the United States is estimated to reach $18–21 billion dollars in 2019 based on historic incidence trends.[19] The cost and benefit of monitoring rather than immediately treating low risk papillary thyroid cancers, the most common type, has been examined in three recent studies. Two concluded that monitoring (termed active surveillance) was superior to surgery from a value perspective, while the third argued that cost effectiveness depends on variability in a patient’s perspective on quality of life.

Using data from Japanese practices where active surveillance has been adopted, authors calculated the cost per patient over 10 years. Comparing active surveillance with and without conversion to surgery to immediate surgery, they calculated that surgery was 4.7–6.5 times more expensive than active surveillance without accounting for conversion and downstream events, and 4.1 times more expensive when accounting for them.[20]

Another group used a Markov decision tree model to calculate cost effectiveness of active surveillance versus surgery using U.S. Medicare cost data. Using the base case of a 40 year old woman with a 9mm papillary thyroid cancer suitable for active surveillance and followed for 20 years total, they determined that active surveillance was less expensive and more effective (less detriment to quality of life) up to 16 years after diagnosis. From 16–20 years after diagnosis, active surveillance cost an additional U.S. $682 per patient, but with a gain of 0.260 quality-adjusted life years. This extra cost is well below the threshold where other medical services are considered cost effective. There was no change in these results in sensitivity analyses adjusting patient age, complication, or rates of progression.[21]

A third group also used Markov decision model analysis, this time to examine the cost effectiveness of active surveillance versus hemithyroidectomy. Again using a base case of a 40 year old with micropapillary thyroid cancer, they determined that active surveillance was less expensive with higher quality of life, but only if the health utility of active surveillance was < 0.01 below that for hemithyroidectomy or life expectancy was less than two years. With increasing belief that active surveillance results in a lower quality of life, hemithyroidectomy, while more expensive, became more cost-effective.[22]

Conclusion

The incidence of thyroid cancer has increased dramatically in recent decades due in large part to identification subclinical disease. The rate of increase may be plateauing, perhaps due to efforts to discourage behaviors that lead to their detection, such as aggressively biopsying small nodules and performing extensive surgeries. For people who are identified with low risk papillary thyroid cancer, the new management strategy of active surveillance holds promise as a potential path to avoid the harms of aggressive treatment while remaining cost effective. Additional research is needed to examine long term outcomes of the active surveillance approach, including oncologic, quality of life, and financial and opportunity costs.

Acknowledgments

This manuscript has been reviewed and approved by all authors.

none.

Financial support and sponsorship: Dr. Davies work is supported by the Department of Veterans Affairs.

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Key points

- The incidence of thyroid cancer has tripled or more in many developed countries over the past 30 years, and this has been attributed to overdiagnosis.
- Recent practice guidelines are encouraging less aggressive evaluation and management of asymptomatic, incidentally identified thyroid nodules.
- For patients who are identified with a low risk thyroid cancer, the option of active surveillance is acknowledged in current guidelines.
- A proposal has been made to remove certain types of thyroid cancer from the list of malignant thyroid neoplasms, specifically encapsulated follicular variant of papillary thyroid cancer.
- Due to recent growing awareness of the problem, the detected incidence and surgical rates appear to be stabilizing in some countries.