

Thyroid Cancer Epidemic: A Peril or an Alarm?

Zahra Nozhat,¹ Mehdi Hedayati,¹ and Feridoun Azizi^{2,*}

¹Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

²Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Feridoun Azizi, Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. E-mail: azizi@endocrine.ac.ir

Received 2015 March 7; Revised 2015 June 9; Accepted 2015 July 8.

Keywords: Epidemic, Cancer, Queensland

Dear Editor,

Thyroid cancer is the most common endocrine malignancy and accounts for roughly 1% of all of human cancer (1). Four main types of thyroid cancer consist of papillary, follicular, and anaplastic thyroid cancers, which stem from thyroid follicular cells, and medullary thyroid cancer, which arises from thyroid C cells (2). Follicular cell-derived cancers and medullary thyroid cancer are responsible for approximately 95% and 5% of all thyroid carcinomas, respectively (3-6). Thus, when compared with other human cancers, a scenario of a thyroid cancer tsunami should seem unlikely. Nevertheless, according to a report from South Korea, the incidence of thyroid cancer has risen 15-fold over the past 2 decades in this country (7). Furthermore, another report from Australia has demonstrated a remarkable increase in thyroid cancer incidence in Queensland (8). Accordingly, the fast growing rate of thyroid cancer is higher than that of any other type of cancer.

In order to consider this problem, we made 2 assumptions: 1) the problem can be assumed as a real dramatic increase in thyroid cancer incidence; therefore, it is crucial to look for biological reasons and/or environmental exposure to specific carcinogens. 2) There is an over-diagnosis or a false positive made by the diagnostic methods and instruments normally used (mainly ultrasound of the neck in the hospital or physician's office). So, the main question in this area is: why has a rare cancer become the most common cancer according to the 2 reports from South Korea and Australia?

First Assumption: Real dramatic increase in thyroid cancer

That the reports from South Korea and Australia on the epidemic of thyroid cancer run against our expectations should not constitute grounds for a hasty confirmation or rejection. However, a significant increase in the screening results of the disease (i.e. diagnosis)

without a concomitant rise in mortality should logically lead to doubts. A burst incidence of thyroid cancer must be preceded by a drastic increase in the incidence of its risk factors. The most important risk factors for thyroid cancer are iodine deficiency and radiation exposure, and there cannot have been a significant change in other risk factors such as age, gender, race and ethnicity, exposure to ionizing radiation, and gene mutations. Changes in some factors such as an increase in the body mass index and/or a decrease in physical activity may amplify the incidence of some diseases such as diabetes. They are not, however, exclusive to South Koreans or Australians and cannot be deemed the principal causes of a real tsunami in thyroid cancer.

Second Assumption: Overdiagnosis of thyroid cancer

Over-diagnosis is the detection and diagnosis of a disease (e.g. cancer) that will never cause symptoms or lead to mortality during an individual's lifetime. In most epidemiologic cancer studies, over-diagnosis has been introduced as an adverse side effect of screening for early forms of diseases. The most salient outcomes of this phenomenon are emotional effects on the individual and unnecessary treatments, some of which can be harmful with irretrievable undesirable effects. Accordingly, the disconcerting figures in the aforementioned reports can be deemed a consequence of the over-diagnosis and false-positive results of some screening programs. As a case in point, the correlation data (16 regions, 2008 - 2009) presented in the report from South Korea can only be a token of the precision of the study, but not its accuracy, because this information is related to the same population, geography, and diagnostic tools. This report can, however, serve as a wake-up call, demanding a doubtful attention to the usefulness of the current methods, guidelines, and available tools for the screening for cancer. A 15-fold increase in detection, if the

screening diagnosis is a false positive or over-diagnosis, is bound to be fraught with psychological, socioeconomic, and ethical problems. Therefore, this report should be viewed with due caution.

On the basis of the reports in NEJM and Clin Endocrinol about the dramatic increase in thyroid cancer incidence in South Korea and Queensland, we assumed 2 likely scenarios: 1) a real dramatic increase in thyroid cancer and 2) an over-diagnosis of thyroid cancer. Apropos the report from South Korea and the claim by Welch et al. that virtually all individuals diagnosed with thyroid cancer are treated roughly two-thirds via radical thyroidectomy and one-third through subtotal thyroidectomy and also with due attention to the definition of over-diagnosis, it can be concluded that the results of the study trend toward over-diagnosis and, thus, cannot suggest a dramatic rise in thyroid cancer incidence in the population under study.

Iran is located in the iodine deficiency area; and although the problem is under control with the use of iodized salt, iodine deficiency may recur with non-contentious survey. Meanwhile, iodine deficiency is an important risk factor for thyroid cancer, so screening for thyroid cancer in this context seems justified. Nevertheless, it is advisable that the possibility of a false positive and an over-diagnosis be taken into consideration in the diagnosis of thyroid cancer with a view to avoiding psychological and socioeconomic consequences.

Authors' Contributions

Study concept and design: Mehdi Hedayati. Acquisition

of the data: Mehdi Hedayati and Zahra Nozhat. Analysis and interpretation of the data: Mehdi Hedayati, Zahra Nozhat, and Feridoun Azizi. Drafting of the manuscript: Mehdi Hedayati and Zahra Nozhat. Critical revision of the manuscript for important intellectual content: Mehdi Hedayati, Zahra Nozhat, and Feridoun Azizi. Statistical analysis: there is no statistical analysis. Administrative, technical, and material support: these items are not related to our study. Study supervision: Mehdi Hedayati.

References

1. Barzon L, Boscaro M, Pacenti M, Taccaliti A, Palu G. Evaluation of circulating thyroid-specific transcripts as markers of thyroid cancer relapse. *Int J Cancer*. 2004;**110**(6):914-20.
2. Wartofsky L, Nostrand V. *Thyroid cancer, a comprehensive guide to clinical management*. Washington: Washington Hospital Center; 2006.
3. Solomon B, Rischin D. Progress in molecular targeted therapy for thyroid cancer: vandetanib in medullary thyroid cancer. *J Clin Oncol*. 2012;**30**(2):119-21.
4. Hedayati M, Nabipour I, Rezaei-Ghaleh N, Azizi F. Germline RET mutations in exons 10 and 11: an Iranian survey of 57 medullary thyroid carcinoma cases. *Med J Malaysia*. 2006;**61**(5):564-9.
5. Hedayati M, Zarif Yeganeh M, Sheikhol Eslami S, Rezghi Barez S, Hoghooghi Rad L, Azizi F. Predominant RET Germline Mutations in Exons 10, 11, and 16 in Iranian Patients with Hereditary Medullary Thyroid Carcinoma. *J Thyroid Res*. 2011;**2011**:264248.
6. Majidi M, Haghpanah V, Hedayati M, Khashayar P, Mohajeri-Tehrani MR, Larijani B. A family presenting with multiple endocrine neoplasia type 2B: A case report. *J Med Case Rep*. 2011;**5**:587.
7. Ahn HS, Kim HJ, Welch HG. Korea's thyroid-cancer "epidemic"-screening and overdiagnosis. *N Engl J Med*. 2014;**371**(19):1765-7.
8. Pandeya N, McLeod DS, Balasubramaniam K, Baade PD, Youl PH, Bain CJ, et al. Increasing thyroid cancer incidence in Queensland, Australia 1982-2008 - true increase or overdiagnosis? *Clin Endocrinol (Oxf)*. 2015.