

Changing natural history of differentiated thyroid cancer

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Published online: 27 June 2012
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The incidence of thyroid cancer has been increasing in many countries over the last 30 years. In the USA, the incidence of thyroid cancer increased from 3.6/100.000 people in 1973 to 8.7/100.000 people in 2002 [1]. This phenomenon is mainly due to an increase in the papillary histotype, which raised from 2.7 to 7.7/100.000, a 2.9-fold increase. The same trend has been reported in Europe [2]. The bulk of the increase is probably the results of better detection of small cancer, measuring 1.5 cm or less. Despite increasing incidence, the mortality from papillary thyroid cancer remained stable (0.5 deaths/100.000 in both 1973 and 2002) [1]. A recent study by Pagano et al. [3] confirm this trend in thyroid cancer patients diagnosed in a tertiary hospital in north Italy, in an area characterized by moderate iodine deficiency. The authors compared the epidemiological and clinico-pathological features of patients according to the time of diagnosis (1997–2005 and 2006–2010). The cut off of 2005 was chosen because it is coincident with the introduction of iodine prophylaxis and with the adoption of international guidelines for the diagnosis and management of thyroid cancer [4, 5].

The main finding is that in more recent years, cancers were diagnosed at an earlier stage, in agreement with the similar observation in other European and North American countries. Increased scrutiny of the thyroid gland, mainly by neck ultrasound, is the most likely explanation for this phenomenon, but the other possibility is that some, as yet unknown, carcinogens in the environment might play a role. Up to now, the only established environmental risk

factor for thyroid carcinoma is exposure to ionizing radiation, and the risk, particularly of papillary carcinoma, is greater in subjects of younger age at exposure, as demonstrated following the explosion of the Chernobyl nuclear reactor in 1986 [6]. According to a network of population-based cancer registries in Italy [7], the temporal trend for thyroid cancer in the period 1988–2002 showed a statistically significant increase of incidence rates in both male and females, that overall showed an annual percent increase of 4.0 % similar to the 3.8 % observed in USA [1]. Based on temporal relationship, it has been claimed that the increase might be a consequence of the Chernobyl fallout. However, no increase in thyroid gland abnormalities, such as nodularity or cancer, was found in northern Italy, among children already born at the time of Chernobyl nuclear accident, when examined 10 years after [8]. This epidemiological evidence does not favor any link between the Chernobyl accident and the increased incidence of thyroid carcinoma in countries other than Belarus, Ukraine, and Russia. Of particular interest is the finding that nearly 20 % of the patients reported by Pagano et al. [3] had an occupational exposure in textile industries. Although the study did not include a control group with the same exposure, the finding recalls a previous Chinese study [9] documenting an association between thyroid cancer and possible exposure to formaldehyde and benzene during long-term employment in textile industries.

Another novel finding of Pagano et al. [3] is that cancers diagnosed between 2006 and 2010 presented more frequent association with autoimmune thyroid phenomena. The last observation might be linked to the augmented iodine intake after establishment of iodine prophylaxis in the country and it is in keeping with the evidence that in countries with high nutritional iodine intake the incidence of autoimmune thyroid disorders is higher compared to countries with

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moderate or severe iodine deficiency. In addition, recent studies indicate that thyroid nodules associated with autoimmune thyroiditis carry a higher risk of malignancy [10]. If this is the case, one might speculate that the increased incidence of thyroiditis might be an additional factor contributing to the increased incidence of thyroid cancer in recent years.

In conclusion the natural history of thyroid cancer is changing. The increasing incidence of thyroid cancer in Italy, as well as in other European countries and in the United states, is likely due to the increased detection of subclinical disease, that would have gone unnoticed without the large diffusion of neck ultrasound in the clinical practice. Whatever the explanation, it is time to explore in deeper the possible impact of environmental agents on thyroid cancer development.

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