

In women, the incidence of thyroid cancer diagnosis is rising at the fastest rate of all malignancies.

New trends in thyroid cancer – a true incidence rise or over-diagnosis?

Thyroid cancer (TC) is the most prevalent endocrine cancer, accounting for about 95% of all such malignancies. The incidence of this cancer has increased dramatically in the last three decades.

Types

Traditionally, thyroid cancers are classified according to their histological cell of origin (see box) as well as whether they are well differentiated (papillary and follicular) or poorly differentiated (medullary and anaplastic), with the latter having a poorer prognosis.

Papillary carcinoma is the most common thyroid cancer (70–80%). It is also the most common type in women and lives under 45. Usually has an excellent prognosis and tends to be localised.

Follicular carcinoma causes about 10% of all thyroid cancers. Typical age of diagnosis is older than the papillary type, and again affects more female lives than male. Hürthle cell carcinoma is an aggressive subtype.

Medullary carcinoma represents about 3–10% of all thyroid cancers. Around 70% of cases occur in older lives (>50). In those younger, it is nearly always associated with a strong family history.

Anaplastic carcinoma is an extremely aggressive tumour that represents less than 5% of all thyroid cancers. It generally occurs in older individuals.

Primary lymphoma represents less than 5% of all thyroid malignancies, with Non-Hodgkin's B cell tumours being the most common.

Causes/risks

Exposure to ionising radiation is the most established direct cause of thyroid cancer, and it was the first solid tumour type noted in Japanese atomic bomb survivors; similar tumours have been seen in areas exposed to radioactive fallout from the test sites in the Pacific as well as in Ukraine in the aftermath of the Chernobyl disaster in 1986. The thyroid is

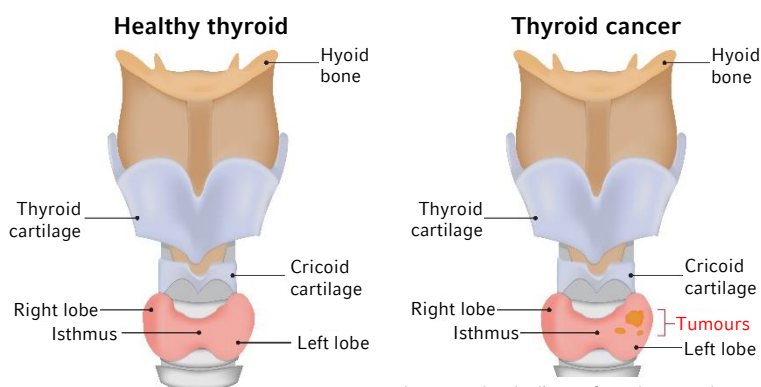


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Healthy thyroid versus thyroid cancer

particularly sensitive to irradiation because it concentrates radioactive fallout iodine as it creates thyroid hormones¹.

Many tools used in medicine also require radiation exposure, notably x-rays and CT scans, and the risk of triggering cancers in later life is particularly problematic in children, with an estimated 1,000 future thyroid cancer cases attributed to undergoing such scans in the US in 2007, for example². Consequently, in many health jurisdictions thyroid shielding is required when undergoing 'routine' but required radiological investigations.

Diet may play a role in two ways: iodine deficiency, if prolonged, triggers a rise in thyroid-stimulating hormone (TSH), which in turn results in more thyroid follicular cell formation. In regions with extensive iodine deficiency, more follicular cell than papillary cell carcinomas are reported. TSH plays a critical role here, as demonstrated by improved survival and reduced recurrence of thyroid cancer in patients treated with TSH suppressors such as L-T4. Obesity and its associated issue of insulin derangement also seem to be distinct risk factors. One study found that 50% of papillary carcinoma patients had insulin resistance. Overall, it appears that for every 1kg/m² in BMI the risk of thyroid cancer increases by 1% and the risk is particularly elevated for females³.

One of the primary functions of the thyroid gland is to produce and regulate the secretions of hormones (thyroxine (T4) and triiodothyronine (T3) used to regulate our metabolism. Given the gender disparity, many researchers have speculated whether other hormones, notably oestrogen and progesterone, could play a part in carcinogenesis in the thyroid gland; recent studies have begun to suggest an imbalance between the two oestrogen receptor (ER) isoforms, α and β , that may indeed be responsible for triggering cellular abnormalities in the gland.

Genetics

Genetic factors also increase the risk for developing thyroid tumours. About 6% of malignant papillary tumours are familial and up to 30% of medullary cancers have a hereditary component. Certain syndromes are associated with a higher likelihood of developing thyroid cancer. These include Gardner's syndrome, Cowden's disease, familial medullary cancer and multiple endocrine neoplasia (MEN) types 2a and 2b⁴.

¹ See IGLESIAS, 2017

² See PELLEGRITI, G. et al., vol 2013

³ See STEELE CB, et al., 2005–2014.

⁴ See BUTLER, C, 2014

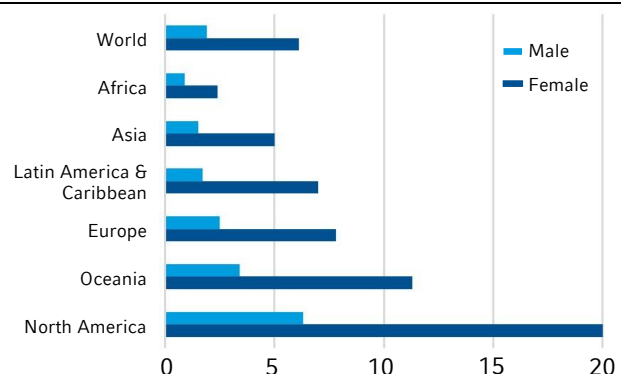
Environmental factors

Other environmental factors, especially chemicals, could explain a rise in mutations – most notably nitrate contamination of drinking water and the use of pesticides such as polybrominated diphenyl ethers, exposure to which may either increase the cancer risk or induce thyroid cell proliferation⁵.

Incidence

Globally, TC is the 16th most common cancer diagnosed, with 298,000 cases diagnosed in 2012; female lives constitute 70–75% of the diagnoses⁶. Curiously, of all cancers that can occur in both sexes it is thyroid cancer (apart from breast cancer) that has the biggest gender disparity. That said however, the cancer presents at a later stage and has a worse prognosis in men.

Figure 1: Global incidence rates for thyroid cancer*



*Age-standardised rates, WHO GLOBOCAN, 2012

Future projections

It is projected that by 2035 the diagnostic incidence rate in the UK will rise by 74% in males and 77% in females, the largest rate of increase across all cancers. However, it will remain a rare cancer in the UK (only 1–2% of all cancer diagnoses), with only around 6,800 people affected, up from 3,388 in 2014⁷.

This pattern of incidence rise is repeated across the world. In the United States the number of cases has tripled since the 1980s to over 57,000⁸, in France rates have increased by 8–9% per year over the same period and in Japan rates have grown by 52% in men and 86% in women in the period

⁵ See PELLEGRITI, G. et al., vol 2013

⁶ See CANCER RESEARCH UK, 2018.

⁷ See CANCER RESEARCH UK, 2018

⁸ See SCHARPF, J., 2017

since the mid-1970s⁹. China has seen the most dramatic rises, where TC is now the second-most frequently diagnosed cancer in both sexes in ages 15–44¹⁰.

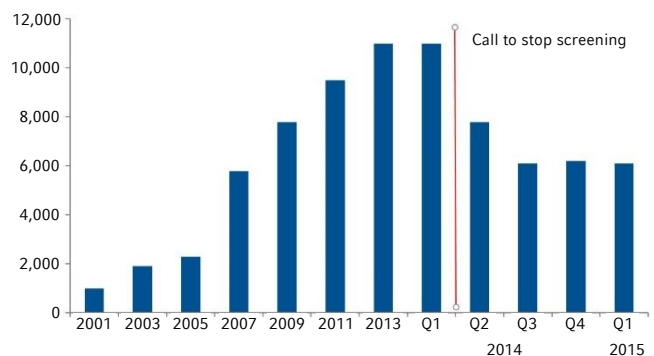
Why?

Over two-thirds of adults will be found to have nodules in their thyroid when undergoing an ultrasound scan (almost all of them are benign), an example of ‘look and you’ll find’¹¹. Therefore, it is perhaps unsurprising that when South Korea introduced a programme in 1999 under which patients could elect to purchase such a service incidence rates of thyroid cancer exploded, with the result that by 2011 the thyroid cancer diagnosis rate was 15 times the rate seen at the beginning of the programme. This prompted a pressure group within the Korean medical community (the “Physician Coalition for Prevention of Over-diagnosis of Thyroid Cancer”) to call for an immediate halt to the screening in 2014, a move which was followed by a decrease in diagnostic incidence of 40% in 3 months¹².

This trend has also been observed globally, with an estimated 50–90% of thyroid cancer (particularly in women) being the result of over-diagnosis. This over-diagnosis has been particularly problematic in countries that rely on an ‘insured model’ of health care provision. Loehrer et al. reported a 26% rise in thyroidectomies to treat thyroid cancer in Massachusetts once the state insurance scheme there was expanded to cover treatment of the disease. In an effort to combat this, the US Preventive Services Task Force (USPSTF) issued a recommendation against screening for thyroid cancer (in particular the use of ultrasonography), stating in effect that the harm from treatments outweighs any long-term benefit.

If the over-diagnosis hypothesis was the only cause of the incidence rise, we should see rates increasing solely in the lower and less aggressive types. Yet the incidence has increased for all types by 3% annually in the last 30 years, with mortality increasing by 1.1% per year for all types and by 2.9% p.a. for advanced-stage papillary in the same period¹³.

Figure 2: Impact of screening in South Korea*



*Korean screening data derived from Hyeong Sik Ahn: Quarterly average number of patients who underwent surgery for thyroid cancer.

Mortality

In the US, the 5-year survival rate for thyroid cancer overall is 98.1% and varies from 99.9% (68% of cases) for localised disease to 55.3% for distant disease (4% of cases)¹⁴.

Papillary thyroid cancer, the most common subtype of well differentiated thyroid cancer, causes nearly 90% of cases, and has by far the best prognosis, with universal 5-year survival and 10-year survival rates of 92–95%¹⁵. In 2007, Pelizzo et al. demonstrated that survival continues into the second decade and beyond¹⁶. However, some histological forms, notably the anaplastic type, cause symptoms, and grow and spread very rapidly. The median survival is 5 months and less than 20% live longer than a year. The 5-year survival rate is around 10%^{17,18}.

⁹ See PELLEGRITI, G. et al., vol. 2013

¹⁰ See WANQING CHEN, et al., 2014

¹¹ See DAVIES, L., 2017

¹² See HYEONG SIK AHN & GILBERT WELCH, H., 2015

¹³ See SOSA, J., 2017

¹⁴ See BIBBINS-DOMINGO K. et al., 2017

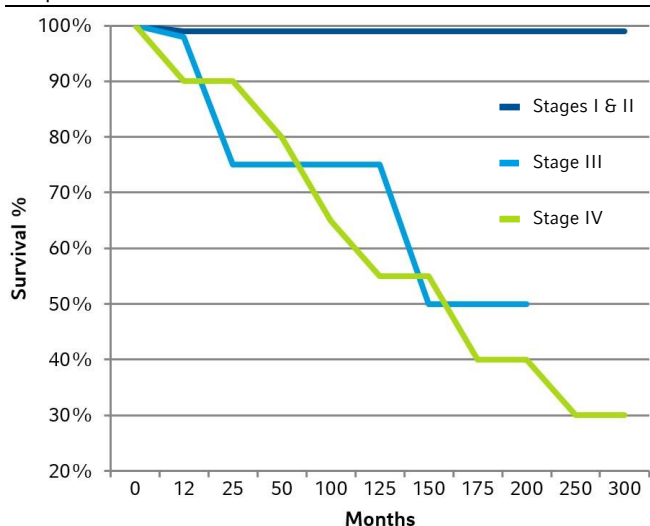
¹⁵ See SOSA, J., 2017

¹⁶ See PELIZZO, M.R. et al., 2007

¹⁷ See BROWN, T, et al., 2012

¹⁸ See O'NEILL, J.P. et al., 2013

Fig. 3: Survival for thyroid cancer by stage
(Kaplan-Meier curves derived from Pelizzo)



Claims

This rise in incidence in the population is being reflected in claims in certain markets, particularly for products like critical illness. This is indeed the case in South Korea given the screening issue discussed above, and it is also evident in China. In China TC accounts for 30–42% of all cancer claims in some portfolios, overtaking breast cancer as the number 1 cause of cancer claims. There is evidence that this trend may also be emerging elsewhere for some CI claim portfolios; in the UK, for example, it is the sixth most common cause of female cancer claims – so at least our experience from the numbers of our branches in Shanghai and UK. It is perhaps unsurprising, then, that the Association of British Insurers is recommending in its 2018 CI minimum standards that stage 1 papillary tumours should be excluded from the cancer benefit.

Conclusion

Product developers, actuaries, underwriters and claims assessors should expect to see thyroid cancer cases with increasing frequency, particularly in markets where pre-symptomatic screening is prevalent. This rise is predominantly a result of over-diagnosis of indolent tumours, although emerging environmental issues may also be contributing to the incidence rise. While certain types of thyroid cancer can be life-limiting and aggressive, in many instances the disease has little impact on life expectancy and should not be considered a ‘critical illness’.

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