Lower TSH and higher free thyroxine predict incidence of prostate but not other common cancers

The pituitary gland signals production of thyroid hormones by the thyroid gland through secretion of thyrotropin (TSH). There are two types of thyroid hormones produced by the thyroid gland. These include thyroxine (T4) and tri-iodothyroinine (T3). These subsequently feedback to the pituitary gland to create a negative feedback loop. In the bloodstream, a portion of T4 and T3 are bound to proteins whilst a small pool remains unbound and are free to act on thyroid hormone receptors. These are known as free T4 (FT4) and free T3 (FT3). At a tissue level, T4 is also converted to T3 which exerts cellular effects of thyroid hormones. T3 has conventionally been known to act on thyroid hormone receptors located in the nucleus of the cell. However, effects of T3 on non-nuclear pathways modulating cellular growth and survival, and pathways affecting blood vessel formation have also been described. It is therefore plausible that thyroid hormones could affect the growth or development of cancer cells, however there is relatively scant data on the effects of thyroid hormones on cancer risk. The presence of anti-thyroperoxidase antibodies (TPOAb) is associated with an increased risk of autoimmune thyroid disease. An increased risk of breast cancer with autoimmune thyroid disease has been implicated in the literature, however results from previous studies are conflicting.

The aim of our study was to assess associations of TSH, FT4 and TPOAb with the risk of any (non-skin) cancer, and other common cancers (including prostate, breast, colorectal and lung cancer) in a group of men and women. We utilized data from the 1994/95 Busselton Health Survey in Western Australia to perform our study. Participants of this survey completed a comprehensive health and lifestyle questionnaire, underwent various measurements and tests, and provided a blood sample in 1994/1995. This was used to measure TSH, FT4 and TPOAb concentrations. Cancer outcomes were ascertained using data linkage to the cancer and death registries in Western Australia over a 20 year follow-up period. Participants were excluded if they were younger than 25 or older than 84 years, if they had a history of previous cancer, if they were taking thyroid-related medications, or if there was biochemical evidence of thyroid dysfunction. In our analyses, we also accounted for other factors which may affect cancer risk such as age, sex, marital status, occupation, smoking, alcohol intake, leisure time physical activity, body mass index, diabetes and menopausal status or use of the oral contraceptive pill (in women only). Participants who died within the first 2 years of follow-up were also excluded.

There was a total of 3649 participants who were included in the final analysis. Of these, 600 were diagnosed with any (non-skin) cancer, including 126, 100, 103 and 41 participants who were diagnosed with prostate, breast, colorectal and lung cancers respectively. After accounting for other cancer risk factors, higher TSH levels (signifying decreased FT4 exposure) was associated with a decreased risk of developing prostate cancer. Similarly, higher FT4 was associated with an increased risk of developing prostate cancer. No associations of thyroid hormones or TPOAb with other common cancers or any (non-skin) cancer was observed in our study.

Our results indicate an increased risk of prostate cancer with increased thyroid hormone exposure. Given the potential for thyroid hormones to modulate cellular growth, metabolism, and blood vessel formation, further studies are required to validate our findings, and to elucidate mechanisms in which thyroid hormones may contribute to prostate cancer growth and development.

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