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COMMENTARY

Re: Thyroid hypofunction in aging testicular cancer survivors

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To the Editor,

We read with great interest the recent paper by Nome and colleagues [1]. In this important study, Nome *et al.* [1] objectively evaluate the prevalence of thyroid hypofunction among a cohort of Norwegian testicular cancer survivors ($N = 727$). They take advantage of results in a normative Norwegian population (the Hunt3 survey) as well as linkage to the Norwegian Prescription Database. Nome *et al.* [1] conclude that 3 decades after testicular cancer diagnosis, the prevalence of thyroid hypofunction (both treated and untreated) was 11% in the testicular cancer survivors, which represented a significant 2-fold increase compared to the normative population (prevalence ratio [PR] 1.91; 95% CI 1.54–2.38). Compared with 148 testicular cancer survivors managed with surgical approaches alone, there was no significant difference in the overall risk of thyroid hypofunction related to the type of cytotoxic testicular cancer treatment (radiotherapy, PR 1.05 [95% CI 0.58; 1.89], $p = 0.152$) or cisplatin-based chemotherapy with/without radiotherapy (PR 1.24 [95% CI 0.69; 2.22], $p = 0.720$). Nome et al. also found no dose-response relationship with cisplatin-based chemotherapy.

Testicular dysgenesis syndrome is an entity that comprises the following four health conditions: poor semen quality, cryptorchidism, hypospadias, and testicular cancer [2]. It has been hypothesized that environmental endocrine-disrupting chemicals may contribute to the development of testicular dysgenesis syndrome by producing insults upon a susceptible genetic background [2]. Evidence suggest that thyroid hormone levels may regulate differentiation of Sertoli cells [3]. By lowering thyroid hormones in rats experimentally, differentiation of Sertoli cells was delayed, leading to decreased numbers of Sertoli cells [3]. Nome *et al.* [1] hypothesize a role for shared etiologic influences, speculating that *in utero* exposure to environmental endocrine-disrupting chemicals may affect thyroid hormones and also contribute to the development of testicular dysgenesis syndrome. This hypothesis may account for the observation that the risk of thyroid hypofunction in TCS managed only with surgical approaches is not significantly different than that observed in the radiation and cisplatin-based chemotherapy with/without radiation groups [1].

What would be helpful in further interpreting the results of their study is the provision of data with regard to the prevalence ratio of thyroid hypofunction (of both of the defined types considered together, and then each presented separately) in the 148 testicular cancer survivors managed only with surgical approaches alone vs. participants in the population-based sample (HUNT3 survey) – along with the absolute numbers of affected TCS/individuals. These results would be helpful to other investigators in the future as they further examine this potential sequelae of testicular cancer and its treatment in other survivor cohorts [4,5].

Nome *et al.* [1] indicate that the findings of this study may have important clinical implications for medical providers who care for testicular cancer survivors. In the Norwegian study [1], approximately 55% ($N = 43$) of testicular cancer survivors with thyroid hypofunction (defined by s-TSH $\geq$3.5 mIU/L) did not receive regular levothyroxine prescription. Due to the association of hypothyroidism with cardiovascular disease [6] and primary hypogonadism [7], future research should examine any relationship of untreated hypothyroidism with the risks of hypogonadism and cardiovascular disease in testicular cancer survivors and further evaluate and quantify the risk of thyroid disease in this vulnerable population.

Disclosure statement

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