Colorectal cancer (CRC) is the third most common cancer in the United States. The causality of CRC is multifactorial and includes genetic factors, lifestyle factors (diet, physical activity, smoking, alcohol consumption), obesity, metabolic syndrome, and sex hormones. In the study by Lu and colleagues published in this issue of Cancer Control, Swedish patients with prostate cancer were followed-up and an increased risk of CRC was observed in patients diagnosed with prostate cancer after 1980, which is when the use of androgen deprivation therapy (ADT; bilateral orchectomy and gonadotropin-releasing hormone [GnRH] agonists) increased in Sweden. No increased risk of CRC was found in patients treated with estrogen therapy. Thus, Lu and colleagues concluded that ADT might be a causal factor for the increased risk of CRC seen in this cohort of patients. The similar but stronger and dose-dependent effect of ADT associated with an increased risk of CRC was also found by Gillessen et al.6

Treatments for prostate cancer include active surveillance, radical prostatectomy, radiotherapy, or hormone therapy. ADT is a first-line treatment option for men with metastatic prostate cancer because it suppresses the binding of androgen to the androgen receptor. In Sweden, hormonal treatment for prostate cancer has changed over time; up until the 1980s, estrogen therapy was the predominant hormonal therapy prior to the introduction of ADT.2

Animal studies have demonstrated that androgen may have a protective effect against colorectal carcinogenesis; by contrast, androgen deprivation may promote it. Evidence indicates that activating androgen receptors represses Wnt/β-catenin/T-cell factor signaling in colon cancer cells and is associated with a decreased risk of CRC. This process may influence competition among androgen receptors and T-cell factors for β-catenin binding; by contrast, administering antiandrogen therapy may instead reverse it. In fact, the expression levels of androgen receptors in CRC are lower than those found in samples of normal mucosa.6 Furthermore, testosterone deficiency has been linked to an increased risk of metabolic syndrome, diabetes, and cardiovascular disease in men; in addition, strong risk factors for CRC include obesity, hyperinsulinemia, type 2 diabetes, and metabolic syndrome.11-16 Research has also indicated that visceral adiposity accumulating during the short-term use of ADT is correlated with resistance to insulin (within 3 months for some cases) and increasing levels of circulating insulin.17

Although clinical recommendations for CRC screening among patients with prostate cancer receiving ADT may be unnecessary at this time, health care professionals should be aware of the association between ADT and CRC in this patient population. It may be advisable for physicians to order relatively inexpensive laboratory studies (eg, fecal occult blood test) and suggest lifestyle modifications and early treatment options for lipid disorders in their patients with prostate cancer receiving ADT.

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References

