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INVITED COMMENTARY

Prostate Cancer

Serum lipid profiles and aggressive prostate cancer

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The introduction of widespread prostate specific antigen (PSA) screening in western countries led to a sharp increase in prostate biopsies and the subsequent diagnosis of prostate cancer. This phenomenon appears to be repeating itself in countries such as China where economic development in recent decades has resulted in increased access to healthcare and more frequent screening tests. It is now recognized that the majority of prostate cancers diagnosed in PSA-screened men is of the indolent nature that does not impact patients' quality of life or life expectancy. Unfortunately, due to our inability to image prostate cancer accurately, biopsies have been performed largely in a blind, un-targeted fashion. Some cancers, particularly those located in the anterior prostate, can be missed with this biopsy technique. On the other hand, if biopsies contain low-grade cancer (e.g. combined Gleason score 6) of limited quantity, it can cause serious difficulties in clinical management. Many such patients have indolent cancers that do not require radical treatments such as prostatectomy or radiation that carry potentially serious side effects. However, a small fraction of these patients actually harbor aggressive cancers that were not adequately sampled by the biopsy. Such uncertainties have resulted in over-treatment as well as under-treatment of patients.

Currently, prediction of the aggressiveness of prostate cancer relies mostly on certain clinical (e.g. preoperative PSA) and pathologic (e.g. Gleason grade and tumor quantities on biopsy) parameters, which is obviously inadequate for certain patients. It is, therefore, important to develop new modalities, particularly noninvasive biomarkers, for better patient management. A study by Zhang *et al.*[1] represents a step forward in this direction. The authors analyzed serum lipid profiles in 322 consecutive patients who received prostatectomy and extended pelvic lymphadenectomy at their institution. Their analysis reveals that total cholesterol, triglyceride, and low-density lipoprotein levels are significant predictors of the pathologic parameters of the tumor after prostatectomy. Specifically, high levels of total cholesterol were associated with increased risk of lymph node metastasis; elevated levels of triglyceride were associated with a more than twofold increased risk of pT3–4 disease, and high levels of low-density lipoprotein were an independent predictor of high Gleason grade (≥8). Importantly, with the increase of the number of abnormal lipid components, a higher probability of pT3–4 disease and lymph node metastasis was observed.

This study thus demonstrates the potential value of serum lipid profile in predicting the aggressiveness of prostate cancer once it is diagnosed by biopsy. Addition of the lipid profile to existing clinical and pathological parameters may increase our ability to determine more accurately which patients may harbor aggressive disease and thus require early intervention. Before this is widely adopted, a few important points need to be raised: (1) this is a retrospective study. A well-controlled prospective study is required to validate the results; (2) this is a single institutional study by a large, well-known tertiary referral center so the potential for bias exists. A larger study involving multiple institutions in different geographic regions with diverse patient populations will provide stronger evidence of the utility of serum lipid profiles in patient management.

In addition to serving as potential novel preoperative biomarkers, the study also provides support to the significance of lipid metabolism in the etiology and biology of prostate cancer. Obesity, physical inactivity, high-fat diet, and dyslipidemia have been considered risk factors for prostate cancer. Prostate cancer cells tend to up-regulate *de novo* lipid synthesis which may contribute to the uncontrolled proliferation of cancer cells. If we consider low-grade, indolent prostate cancer as a normal aging process that occurs in a significant portion of aged men, there may exist different biologic pathways that lead to the development of aggressive prostate cancer, a truly life-threatening disease. Future studies will further pinpoint the exact role of lipids in this disease process.

Although serum-based biomarkers remain a useful research direction, validation of any novel biomarkers and their widespread adoption will take a significant amount of time, effort and resources. On the other hand, improving the radiologic detection of prostate cancer and targeted biopsy of prostate cancer will likely yield more immediate benefits. There has been significant advancement in the detection of prostate cancer, particularly those of high grade and/or high volume, by multiparametric magnetic resonance imaging (MRI). Although MRI-guided biopsy remains an option, targeted biopsy of the prostate using MRI-ultrasound fusion technology appears more practical.[2] With continuous improvement in the technology, we may eventually be able to detect clinically relevant diseases while ignoring indolent ones, resulting in more optimal management strategy for men diagnosed with prostate cancer.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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