May 31, 2014

Dear Editors,

Our revised manuscript has been submitted electronically (Name of file: ESPS Manuscript No. 10021-Review).

Title: Metabolic Syndrome in the Development and Progression of Prostate Cancer
Authors: Andrew C. Strine, Kevin R. Rice, Timothy A. Masterson
Name of Journal: World Journal of Clinical Urology
ESPS Manuscript No.: 10021

Our manuscript has been revised based on the comments of reviewers:

1. Its format has been updated in accordance with the specifications of the journal.
2. The following revisions have been made or addressed:
    a. We specifically did not discuss the role of lipid metabolism in the development and progression of prostate cancer. The aim of our review was to focus on the existing clinical evidence and subsequent implications on the management of prostate cancer, not the molecular or pathophysiologic pathways involved in the metabolic syndrome as well as the development and progression of prostate cancer.
    b. We included a more critical discussion in certain sections, while also being cognizant of the broad nature of this subject and length of our manuscript. We already discussed all relevant meta-analyses to assist with synthesizing the large number of studies and identifying any true associations. We also provided a summary of relevant studies as well as our analysis and recommendations at the conclusion of most sections.
    c. We included more detailed information about the ages of men and aggressiveness of disease in cross-section and longitudinal population-based cohort studies when available. A majority of studies investigating the association between the metabolic syndrome and prostate cancer did not provide any information on the aggressiveness of disease. We also included a table with more information on each study at the conclusion of our manuscript.
    d. In the section on the metabolic syndrome and risk of prostate cancer, we often reported the association between the cumulative number of metabolic components and development of prostate cancer. Unless particularly interesting, we reserved any discussion on each individual component for their respective sections.
    e. We did not include the normal ranges of serum studies due to the use of various definitions among the studies reviewed in our manuscript. This was actually one of our critiques of the current literature, which weakened any comparisons due to the use of various and modified criteria for the metabolic syndrome. We referred to serum studies as “high,” “normal,” or “low” to facilitate the understanding of our audience. We also included a table with criteria for the clinical diagnosis of the metabolic syndrome at the conclusion of our manuscript.
    f. We included a complete list of abbreviations used in our manuscript.

g. Although the genetic differences and dietary variations among various populations may impact the development and progression of prostate cancer, the studies reviewed in our manuscript did not allow for a critical discussion on these subjects.
h. We did not discuss the potential molecular targets for the treatment of prostate cancer in men with the metabolic syndrome, as this was beyond the scope of our review. We only focused on the pharmacologic treatments with promising clinical evidence in humans.
i. We included the normal range of vitamin D levels and age of men participating in the study on the association among the metabolic syndrome, vitamin D level, and prostate cancer. These men did not undergo a bone density scan and were not being treated for low vitamin D levels.
j. We did not include a more thorough discussion on the role of testosterone in the development and progression of prostate cancer, as the audience targeted by our review is already assumed to understand the context in which it is being written.
k. We included or addressed the requested information on the studies investigating the effect of weight loss and exercise on the development and progression of prostate cancer.

3. Our references have been updated in accordance with the specifications of the journal.

We appreciate the comments of reviewers and look forward to your response.

Sincerely,
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