Dear Editor,

I appreciate the author’s response to my previous concerns. However, a few minor issues have arisen that I would like to address point by point, referencing both my previous comments and the authors' responses where necessary:

1. **Clarity on Insulin Resistance and Prostate Cancer Association:**

   My last comment: “The authors should provide more explicit clarification when stating, "However, the association between insulin resistance and prostate cancer is currently uncertain." This statement should be accompanied by a citation supporting their argument and a summary of the existing evidence regarding insulin resistance and prostate cancer, explaining why it is uncertain. Are there inconsistencies in the results of studies? Or is there a lack of evidence regarding this association?”Author’s response: “...We explain the issue "the association between insulin resistance and prostate cancer is currently uncertain" in detail in the introduction…”

   I appreciate the addition of this information in the introduction. However, I suggest summarizing this section (lines 59-93) and clearly delineating the gap in the literature regarding this association and how this study contributes. For instance, one limitation of previous studies on the association between metabolic syndrome components and prostate cancer is the variability in criteria used to identify these conditions. Does this study improve upon previous approaches in evaluating insulin resistance?

2. **Study Population Criteria**

   In the study population section (lines 112-126), the inclusion and exclusion criteria for cases and controls could be collapsed. For example: both groups included participants with any type of cancer or history of cancer; (2) participants with a history of diabetes mellitus and the use of glucose-lowering drugs; (3) participants with a history of diseases related to lipid metabolism disorders, such as liver or

kidney disease, and the use of triglyceride-lowering drugs. included participants without any history of cancer.

3. **Relevance of Prostate Biopsy Details:**

The detailed information about prostate biopsy as a diagnostic method is excessive and may not be relevant. It is enough to mention in the study population section: ""“ We extracted patient information from the Department of Urology of the First Affiliated Hospital of Xinjiang Medical University in 2023, patients diagnosed histologically for the first time with prostate cancer by prostate biopsy

4. **Addressing Potential Confounding Factors:**

It appears that obesity plays a crucial role (line: 275-286-, line 298-314) in elucidating because insulin resistance might be associated with a lower frequency of prostate cancer. Obesity could act as a confounder and an effect modifier, but the logistic regression models were not adjusted by obesity (lines 171-175): “We constructed three logistic regression analysis models to analyze the relationship between METS-IR and prostate cancer. Model 1 did not adjust for any covariates; Model 2 was adjusted for age based on Model 1; Based on Model 2, Model 3 adjusted for hypertension, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), blood calcium (Ca), and alkaline phosphatase”

I suggest adjusting the models by obesity and possibly conducting a sensitivity analysis to evaluate the association across different levels of obesity. Furthermore, in considering whether overnutrition plays a role in this association (lines 297-306), adjustment by energy intake may be necessary. However, in the absence of such data, this limitation should be addressed in the discussion."

5. **Presentation of Results:**

Table 2 and Figure 2 appear to present overlapping information. I suggest keeping only the table or the figure.