

ESPS PEER-REVIEW REPORT

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Title: Insulin-like growth factor-1, IGF binding protein-3, and the risk of esophageal cancer in a nested case-control study

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an interesting and valuable article in exploring the association between esophageal carcinoma, IGF1 and IGFBP3. This is the merit and value of the paper that can be referred and cited by other studies in future when the results are found. However, there are several concerns that should be clarified. It is the concern on the mater for the interested readers who can be involved in this research and can repeatedly practice it in future. I here illustrate some that are unclear, non-understandable, and non-readable letting shortcomings clearly limit the contribution of the paper. Major concerns: 1. In Discussion (page 10), authors addressed that In this study, neither serum levels of ?? IGF1 nor IGFBP3 were related tothe OR for esophageal cancer. However, in Results(page 8), I see that the mean serum level of IGFBP3 was significantly lower in the cancer group than in the controls, see Table 1. 2. A flow chart regarding the research method is required for readers to take a quick glance at the overall research perspective so as to know the nested exploration researches in this study. For instance, I summarized the four tables as below: Table 1: Significance found in IGFBP3 between groups Table 2: In overall perspective, we have not found any significance among three tertile groups

including those adjusted life styles and using single variable logistic regression. Table 3: Ratio method was not significant in tertile groups, but significance was found using the subtraction method. Table 4. Male and age below 65 were found in difference using subtraction method. 3. Authors described in page 11 that as serum IGF1 levels were higher in viscerally obese patients with esophageal cancer than non-obese patients[21, 37], visceral obesity may influence the IGF axis. In page 10, I also see that the molar level of IGFBP3 is higher than that of IGF1. Why we cannot assume that the two have the BMI-like relation. That is to study whether the value of $\text{IGF1} / \text{squared (IGFBP3/100)}$ can predict the risk (or cancer development) of esophageal carcinoma. That is, we expected the relation such as using the formula of $\text{IGF1} / \text{squared (IGFBP3/100)}$ to test whether any significance is existed between groups. 4. Usually, we test variables that are statistically significance first, and then put them into study. That is, we see the two variables should be significant in Table 1. If so, we can confirm and be confident that any changes we design in a study, no mater we use subtraction or ratio method or even the formula of $\text{IGF1} / \text{squared (IGFBP3/100)}$, should be reached at a common conclusion that a significance is found. As for the study, we have not seen all variables that are together with a statistical significance between groups. The following studies or explorations are usually not important as we expected. The findings in this study, such as male and age under 65 or the subtraction method between IGFBP3 and IGF1, are significant and meaningful, are the occasional result of exploration, not in certainty. When we apply it to other samples or with different sample size, the result will be different. That is no enough to make any inference. 5. The baseline survey was conducted between 1988 and 1990. Whether any institute review board (Ethics approval and consent to participate) was involved in this study is required to declare. 6. A total of 31 cases and 86 control subjects were eligible for the present analysis. Availability of data and materials are required to disclose in an appendix because data are small or are drawn with a scatter plot(IGF1 on X axis and IGFBP3 on Y axis) classified with two groups to see the relation of both variables. Readers can see whether IGF and IGFBP form a complex in a 1:1 molar ratio, or the molar level of IGFBP3 is higher than that of IGF1. Minor concerns: 1. The first paragraph In Results(in page 8) revealed that there are three terms regarding groups of case, cancer, and control. Authors should