

ANSWERING REVIEWERS



September, 4, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4962 revision.doc).

Title: Visceral Obesity and Colorectal Neoplasia

Author: Eun Kyung Choe, Donghee Kim, Hwa Jung Kim, Kyu Joo Park

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4962

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

-The manuscript had been edited for English language by American Journal Experts and the certificate has been uploaded.

-The author affiliations have been changed according to the format of the journal

-The results section of the abstract has been expanded to 248 words. The relevant statistical data and percentages have been added.

- Key words has been added to 6 words.

- Core tip has been added

- Comments have been added.

- Figure montages are being submitted in power-point format to make them decomposable. The editor would be able to edit and move the images individually.

2. Revision has been made according to the suggestions of the review

(1)Please explain how diabetes or insulin levels (which are known to influence colorectal cancer prevalence)

do not explain your results, rather than obesity per se.

Reply: Diabetes, one of the factors comprising metabolic syndrome, is also considered a risk factor for CRC. Some studies have shown positive association between diabetes and CRC, while others have shown inconclusive. Our data did not show diabetes was associated with colorectal cancer because our study only included early colorectal cancer. Recent study demonstrated that colon cancer risk is increased in diabetic men before diabetes onset. Diabetes did not alter colon cancer risk in men or women after clinical diabetes onset. In pre-diabetic men, colon cancer risk increased as time to diabetes onset decreased, suggesting that the effects of the pre-diabetes phase on colon cancer risk in men are cumulative.(PLOS one vol 8 issue 8, e70426, Increased Risk of Colon Cancer in Men in the pre-diabetes phase)

Therefore, we have analyzed impaired fasting glucose status together with diabetes as a single covariate. The result has shown in the Table 1 as below.

Table 1. Impaired fasting glucose (IFG)/Diabetes and the risk of colorectal cancer vs. colorectal adenoma and control

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
CRC vs. Control						
IFG / Diabetes	1.60 (1.08-2.37)	0.019	1.54 (1.04-2.29)	0.032	1.66 (1.11-2.48)	0.013
CRC vs. Adenoma						
IFG / Diabetes	1.59 (1.07-2.37)	0.020	1.62 (1.09-2.41)	0.017	1.86 (1.23-2.80)	0.003

^aMultivariate model 1 was adjusted for current smoking status, and alcohol consumption.

^bMultivariate model 2 was adjusted for BMI, in addition. Since VAT and SAT showed co-linearity to BMI, it was not included in the analysis.

^cMultivariate model 3 was adjusted for SAT and VAT, in addition. Since BMI showed co-linearity to adipose tissue amount, it was not included in the analysis.

Multivariable analysis showed impaired fasting glucose/diabetes is an independent risk factor of early colon cancer. We have included these results in the discussion.

“Recent study demonstrated that colon cancer risk is increased in diabetic men before diabetes onset.

Diabetes did not alter colon cancer risk in men or women after clinical diabetes onset. Because we only included patients with early CRC, we thought abnormal glucose metabolism, including impaired fasting glucose and diabetes all together, was a risk factor for early CRC. Multivariable analysis showed impaired fasting glucose/diabetes is an independent risk factor of early colon cancer (data was not shown).

(2)Authors ought to emphasis that conflicting results are due to methods to determine visceral or subcutaneous fat extension. Among them, the fat area is the worst one. It is much better to measure the max lenght from a fixed point. Anyway, Authors should be congratulated on their effort to delucitate this intriguing issue.

Reply: As reviewer’s comments, volumetric measure of visceral adipose tissue was more accurate than visceral adipose tissue area measurement. However, the technique we used for visceral adipose tissue area measurements has been standardized and validated in previous studies. We have commented these content and limitation in the discussion.

“Sixth, volumetric measure of visceral adipose tissue was more accurate than visceral adipose tissue area measurement. However, the technique we used for visceral adipose tissue area measurements has been standardized and validated in previous studies (References as below).

- International journal of obesity and related metabolic disorders 1995; 19(7): 464-467. Reproducibility of computed tomography measurement of visceral adipose tissue area.
- The American journal of clinical nutrition 1988; 48(6): 1351-1361. Total and visceral adipose-tissue volumes derived from measurements with computed tomography in adult men and women: predictive equations.
- Measuring body fat distribution and content in humans. Current opinion in clinical nutrition and metabolic care 2002; 5(5): 481-487.
- The American journal of clinical nutrition 1988; 48(4): 936. Abdominal composition quantified by computed tomography.
- The American journal of clinical nutrition 1982; 36(1): 172-177. Assessment of abdominal fat content by computed tomography.

(3) 1. Please defined "over obesity" in your study. for example, BMI > 30 or 33 or.. 2. Just as the discussion section statements: WC and WHR have shown a stronger positive relationship in the development of colorectal neoplsia. Would you consider included the WC and WHR data and analysis in your article? 3. The table 1 should included the obesity data (BMI) 4. For the HDL-cho, LDL-cho or even the metabolic syndrome are all relevant to central obesity, do you consider give these data (especially the metabolic syndrome) and analysis in your article?

1, 3. BMI classification was included in the Table 1. BMI classified as normal (BMI <22.9), overweight (BMI ≥23.0, <24.9), obese (BMI ≥25.0, <29.9), over obesity (BMI ≥30.0) according to WHO Asian-Pacific guideline.

2, 4. Due to our retrospective study design, we could not take into consideration about the relationship of metabolic syndromes in analysis because data such as triglyceride, HDL cholesterol, and insulin level, were not available. In addition, we did not have data such as WC or WHR in patients with CRC due to our retrospective study design. We have mentioned these limitations in the discussion.

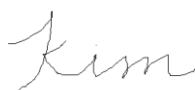
3 References and typesetting were corrected

-Typesetting of headings has been change per the format of the journal.

-References have been added and the orders and numbering have been changed.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



Donghee Kim, M.D., Ph.D

Department of Internal Medicine

Seoul National University Hospital, Healthcare System Gangnam Center

Seoul, 135-984

Korea

Fax : 82-2-2112-5635

E-mail: messmd@chol.com