

Dear Dr. Andrzej S Tarnawski

“Different risk factors for advanced colorectal neoplasm in young adults”

Co-authored by Ji Yeon Kim, Yoon Suk Jung, Jung Ho Park, Hong Joo Kim, Yong Kyun Cho,
Chong Il Sohn, Woo Kyu Jeon, Byung Ik Kim, Kyu Yong Choi and Dong Il Park

Thank you very much for giving us an opportunity for revision.

Accurate and kind comments by the reviewer have been addressed in the discussion. We also believe that these comments improved and clarified our manuscript. Changes have been made by changing the color to **RED** in the revised manuscript to avoid any confusion.

I'm looking forward to good response.

Thank you!

Sincerely,

Reviewer 1

The manuscript described the risk factors for advanced colorectal neoplasm (ACRN) in young Korean adults included age, male gender, current smoking, family history of CRC, DM, obesity, LDL-cholesterol and CEA. Age, male gender, current smoking, obesity and CEA were the risk factors for ACRN in Korean adults older than 50 years age.

Bias exists in the selection of subjects enrolled in the study, which excluded subjects had history of previous colonoscopy, especially in the older age group. Therefore, subjects who had previous colonoscopy should be classified according to age group and numbers be given.

Answer: Thank you for important comment. Around 20% of initial subject in YA group and around 30% of initial subject in OA group were excluded because they had previous colonoscopy. The authors targeted subjects at their first screening colonoscopy to assess the average risk of ACRN. Therefore, high risk subjects with a family history of CRC in the OA group might be missed. These could effect on the study as a selection bias. However, subjects who had previous colonoscopy is heterogenous group including subjects with ACRN, subjects with low risk adenoma or subject with normal colonoscopy. It is also difficult to assess the result of previous colonoscopy relying on subject's memory. Therefore, the authors excluded the subjects who had previous colonoscopy to prevent the heterogeneity of study subjects. We described this as below:

“Around 20% of initial subject in YA group and around 30% of initial subject in OA group were excluded because they had previous colonoscopy. The authors targeted subjects at their first screening colonoscopy, so high risk subjects with a family history of CRC in the OA group might be missed. These could effect on the study as a selection bias. However, the present study aimed to assess the average risk of ACRN. Subjects who had previous

colonoscopy is heterogenous group including subjects with ACRN, subjects with low risk adenoma or subject with normal colonoscopy. It is also difficult to assess the result of previous colonoscopy relying on subject's memory. Therefore, the authors excluded the subjects who had previous colonoscopy to prevent the heterogeneity of study subjects.”

Adenoma detection rate is a quality indicator of colonoscopy and should be provided in the manuscript.

Answer: Thank you for important comment. Adenoma detection rate of the present study is 14.2%. The rate is slightly low when it is compared with recommended adenoma detection rate. However, the present study targeted subject who took first colonoscopy and the majority of subject were young-adult with under the age of 50. This could make adenoma detection rate relatively low. We described this as below:

“Adenoma detection rate of the present study was 14.2% and the rate was slightly low when it was compared with recommended adenoma detection rate. However, the present study targeted subject who took first colonoscopy and the majority of subject were young-adult with under the age of 50. This could make adenoma detection rate relatively low.”

When polyps were found during colonoscopy in the study population, How to treat these lesions in the study? And how to estimate the size of the polyps?

Answer: Thank you for the comment. The size of the polyps was estimated by colonoscopist during the exam. Small polyps 5mm and less were removed by biopsy during the exam. Large polyps larger than 5mm were referred to therapeutic colonoscopy specialist

and removed by endoscopic mucosa resection. And the lesions which cannot be treated by endoscopic procedures were referred to surgery. We explained this as below:

“The size of the polyps was estimated by colonoscopist during the exam.”

Reviewer 2

1. How is it possible the “experienced colonoscopist” were “unaware of the subjects’ clinical features”? It seems virtually unethical for the colonoscopist to be a technician without knowledge of the patient’s condition. Perhaps the language could be refined.

Answer: Thank you for accurate comment. Colonoscopists did not know about the present study when they examined colonoscopy. The authors revised the sentence as below:

“Colonoscopies were performed by experienced colonoscopists unaware of the present study.”

2. The authors state that “CEA increased the risk of ACRN in the OA group”. I am unsure how CEA can cause ACRN although the finding of elevated CEA in patients with ACRN certainly seems legitimate. Again, the authors could potentially reword this explanation.

Answer: Thank you for accurate comment. CEA dose not increases the risk of ACRN, whereas, increased CEA level was resulted by ACRN. The authors revised this as below:

“Serum CEA levels (OR 1.05, 95% CI 1.01-1.09, $P = 0.022$) also related with the risk of ACRN”

3. The authors state that the in the OA group age is a factor for ACRN. It seems self-evident that age would always be a risk factor in older patients.

Answer: Thank you for the comment. In both old-adult and young-adult group, age was revealed as an important risk factor of ACRN regardless of sex. Therefore, the authors explained this in discussion and advocated general colon cancer screening policy which begins at 50 years of age.

The authors appreciate the reviewer's comments. Revision based on these comments has undoubtedly improved the clarity and accuracy of our manuscript.

Dong Il Park, M.D., Ph.D.

Ji Yeon Kim, M.D.