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Risk Factors of Colorectal Carcinoma Incidence in Young Adults: A Meta-analysis

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Abstract

Introduction. The incidence and mortality of colorectal cancer (CRC) in young adults (below the age of 50 years) has been increased. However, there's no screening method for these cancer in those group of age because there is no scientifically proven risk factor. Thus, a meta-analysis carried out to find out the risk factor for CRC in young adults.

Method. A Meta-analysis study was conducted in January 2017. Literature search addressed to the articles published during a period of 2007–2017 in Cochrane and PubMed using keywords: “young” AND “risk factor” AND “colorectal cancer” OR “colon cancer” or “rectal cancer”. Inclusion criteria were the CRC prevalence, risk factor analysis for CRC incidence and young population (below 50 years old). The meta-analysis carried out through qualitative and quantitative approach.

Results. In the last 10 years, there were twelve published articles met the criteria. Those were cohort study (an article), case-control study (four articles), and cross-sectional study (seven articles). Twenty-five risk factors were noted. The meta-analysis showed that gender (males) with OR = 1.66, 95% CI = (1.04–2.64); I₂ = 93%), family history with OR = 2.01, 95% CI = (1.11–3.67); I₂ = 78%), metabolic syndrome with OR = 1.80, 95% CI = (1.49–2.16), I₂ = 0%), and smoking with OR = 1.57, 95% CI = (1.40–1.77), I₂ = 4%) were the significant risk factors with the association of CRC.

Conclusion. Young adults of males, with a family history of CRC, metabolic syndrome, and smoking were at the risk to have colorectal cancer.

Keywords: *colorectal cancer, risk factor, young adults*

Introduction

Colorectal carcinoma (CRC) places the third most common malignancy in the world, following breast and lung cancer.¹ Mostly the population was those who live in the developing country, including Indonesia. According to GLOBOCAN 2012, the incidence of CRC in Indonesia was 12.8 in 100.000 adults, with 9.5% mortality within all cases. The incidence and mortality of CRC decreased in adult older than 50, although increased in adult younger than 50.²

Colorectal carcinoma is classified as familial or hereditary, and sporadic type. Over 85% of CRC incidence is the sporadic type. In the well-developed country, a younger patient with CRC was a hereditary type or the hereditary non-polyposis colorectal cancer (HNPCC) that comprise 5% of the population.³ CRC in young adults was reported to have an even higher incidence in Asian and African populations reaching up to three to four-fold higher than in the well-developed countries.³

Reports showed that CRC in those below 45 years old in Jakarta, Bandung, Makassar, and Padang has an incidence of 47.85%, 54.5%, 44.3%, and 48.2%, respectively. Mostly, these patients were looking for medical service as the disease goes to advanced; of which, does not well respond with chemotherapy. Advanced malignancy in this age group has an impact on productivity and financial problems.³

In general, CRC is related to the interaction of defective genetic predisposition and multiple environmental factors. The genetic predispositions of CRC were not a modifiable risk factor that may be identified by the familial history of CRC or colorectal polyp. The environmental factors were considered as the modifiable factors such as sedentary lifestyle, obesity, high consumption of red meat, smoking, and moderate-high consumption of alcohol.⁴

Nowadays, the screening method for CRC is addressed for the adult patient (>50 years old). The risk factor on the guidelines is a risk factor that is suited for all ages, particularly the elder.² There were many articles focused on the risk factors for CRC in young adult, but no meta-analysis found. Thus, the study aimed to provide scientifically proven risk factors for CRC in young adults. The recognition of these risk factors is an important key for strategic management, namely the prevention, early diagnosis, and prompt treatment.

Method

A meta-analysis study carried out to find out the risk factors of CRC in young adults in accordance with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA–2015). The study conducted in Digestive Surgery Division, Department of

Surgery, Faculty of Medicine, Universitas Indonesia, dr. Cipto Mangunkusumo General Hospital, 2017.

The literature search carried out in the online database (Cochrane and PubMed) using keywords: “young”, “risk factors”, “colorectal/colon/rectum/cancer/carcinoma/adenocarcinoma”.

Eligible studies to the analysis were those published within the last 10 years, including prevalence and risk factors of CRC, and age group below 50 years. Those were excluded if risk factor value (odds ratio) were not included in the article. The quality of the qualified studies assessed by subject characteristic, year of publication, place of the study, and results of each study. Odd ratio with 95% confident

interval that measuring the correlation between risk factors and CRC was obtained and calculated by MetaXL version 5.3 software. Health state Quality Index was obtained from each of the studies. The quality impact model was then obtained using software to reduce heterogeneity caused by the variability of quality from these studies. The homogenous studies then analyzed by a fixed-effects model and heterogeneous studies were analyzed using a random-effects model. The publication bias was evaluated by the Funnel plot, which was a natural logarithm of odds ratio was plotted against the inverse of standard error. The result was presented by the Forest plot.

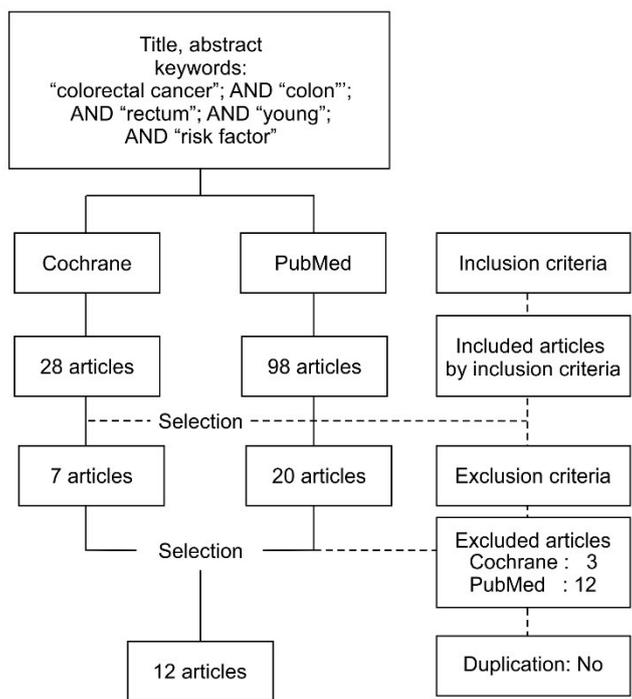


Figure 1. A literature search in the study

Results

There were 124 articles identified during searching from 2007–2017. All abstracts were scanned and a total of 22 full articles reporting the risk factors of CRC were selected. Twelve full articles were met with inclusion and exclusion criteria without duplication. Selected articles were observational studies with a cohort study, four case-controlled studies, and seven cross-sectional studies. Detailed steps of article selection presented in figure 1.

The age group of the population was found in the range of 19–49 years. Twelve full articles were enrolled in this study: nine studies

conducted in South Korea. All population was evaluated by colonoscopy and the risk factors were evaluated by interviews, questionnaires, or medical records. The risk factors were then correlated with the findings of colonoscopy were confirmed by histological examination.

Twenty-five risk factors were noted from the articles were listed in table 1. The selection was carried out and found a total of six risk factors that included in at least three studies. Two risk factors were excluded due to incomplete data. The risk factors that included, in the final analysis, were gender (males), family history of CRC, metabolic syndrome, and smoking.

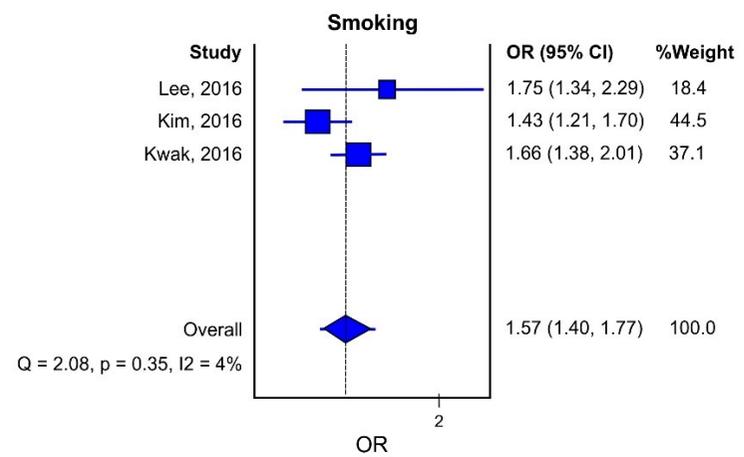
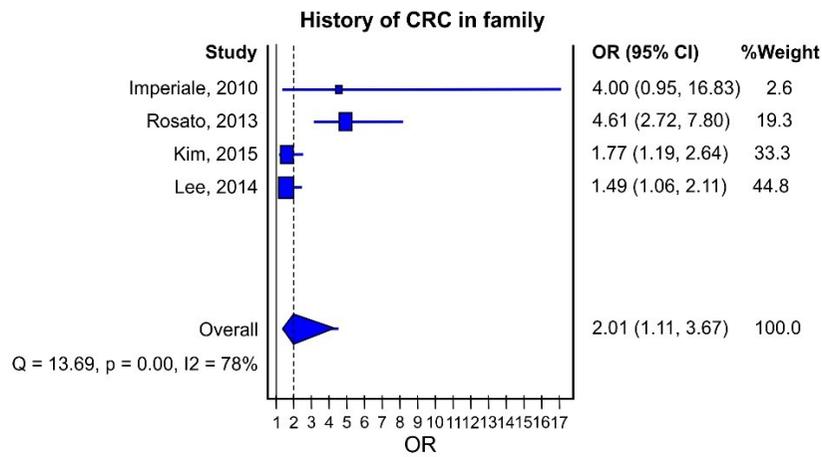
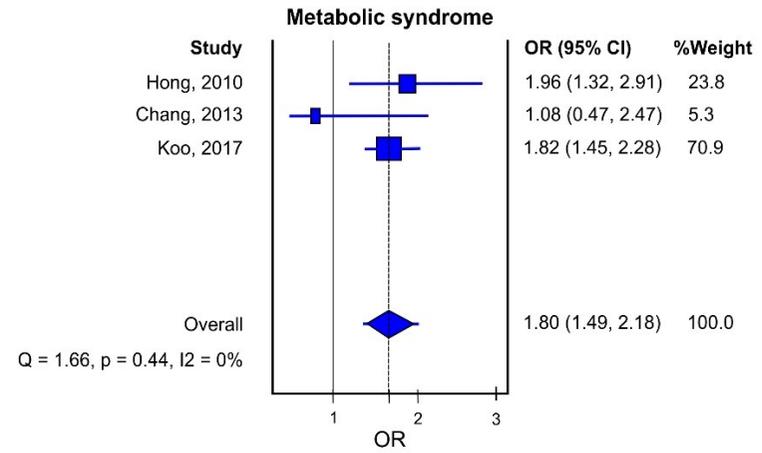
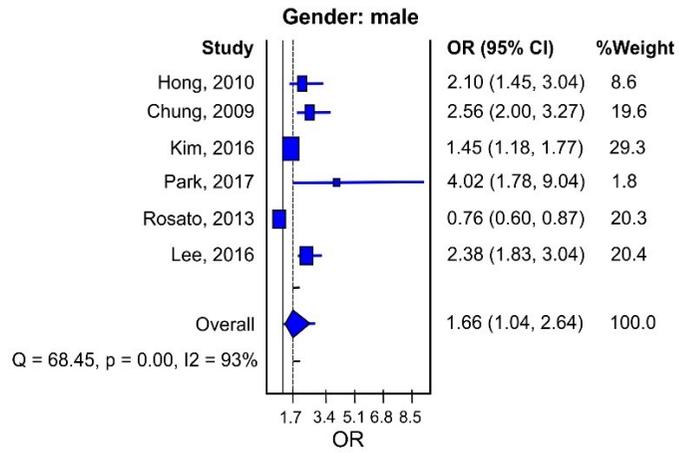


Figure 2. Forest plot of the risk factors

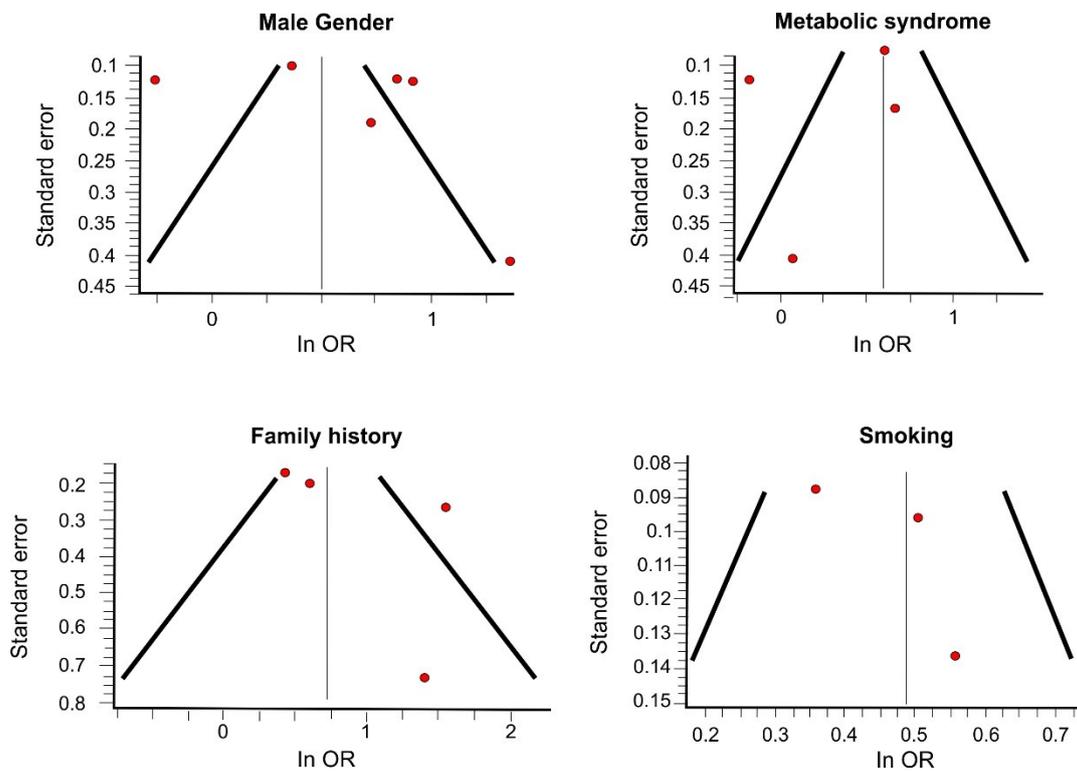


Figure 3. Funnel plot of the risk factors.

Discussion

The aim of this meta-analysis was to find out the risk factors of CRC in young adult below 50 years of age. Based on the 25 risk factors identified in the articles, only a total of six factors were qualified to be included in this analysis, which is, family history of CRC, gender (males), metabolic syndrome, alcohol consumption, obesity, and smoking. These risk factors were analyzed and presented in figure 2. Two of these risk factors (alcohol consumption and obesity) were excluded due to incomplete data and could not proceed for the analysis.

The final analysis for male gender showed a significant statistical result with $OR=1.66$; $CI = 1.04-2.64$; $I^2 = 93\%$. Male gender was reported in six studies, the most risk factors included in this study. Comparison for this risk factor was made with systematic review by Nguyen et al. Their study showed a relative risk of 1.83 (95% $CI = 1.67-1.91$) in every age group. Although relative risk and odds ratio cannot be compared equally, both studies showed male gender increase the risk of the development of CRC in young adults. The etiology of this factor had not yet been clearly identified. McMichael and Potter proposed hormonal difference between male and female as a potential cause as cited by Nguyen.¹⁸ It was their study that proposed the role of estrogen and progesterin in preventing CRC.¹⁸ Lifestyle difference between male and female, especially in relation to alcohol consumption and smoking habit were also believed to be related to increased risk in the male gender. Others proposed genetics differences as a possible cause, yet it was not concluded in this study.¹⁸

Family history of CRC is also a statically significant risk factor for CRC in young adults with $OR=2.01$; 95% $CI = 1.11-3.67$; $I^2 = 78\%$. Heterogeneity of family history of CRC outperform the other risk factors. A young adult with a first-degree family member diagnosed

with colorectal adenoma or invasive colorectal cancer has increased the risk to develop colorectal cancer. Lowery et al also found a similar result with the risk of developing CRC doubles in population aged above 60 and triples in population below 50. This study shows an even greater risk compared to this study.¹⁹

This study also found the metabolic syndrome as a risk factor for CRC with $OR = 1.57$; 95% $CI = 1.40-1.77$; $I^2 = 4\%$. Metabolic syndrome is a modifiable risk factor consist of obesity, hypertension, hyperglycemia, and dyslipidemia. The syndrome has spread up to each age group as the lifestyle changes from the Western culture to the Eastern culture.¹⁵ The relation of metabolic syndrome with CRC was also found in the study of Alfa-Wali et al (2015), who found a strong correlation between metabolic syndrome and CRC. The study shows $OR = 1.51$; 95% $CI = 1.32-1.73$, which was highly similar to this study. However, the pathogenesis of metabolic syndrome with CRC remains investigated.^{15,20}

Smoking was also showed significant statistically with $OR = 1.57$; 95% $CI = 1.40-1.77$; $I^2 = 4\%$. In these studies, the population that considered smoking were a current smoker who had smoked for the last one year and remains to smoke. The duration and frequency of smoking were not considered in these studies. The previous study of Limsui as cited by Chang (2014) showed smoking as a risk factor for CRC by systematic review on 25 cohort studies with $RR = 1.12$; 95% $CI = 0.86-1.46$.¹⁵ Bias for publication was not found in this study which proven by the Funnel plot (figure 3).

The study encountered some limitations. Firstly, the difference of operational definition found on some risk factors that may lead to bias, although those studies were not included in the final analysis. Secondly, most of the studies included in the analysis were carried out in South Korea. Thus, external validation of the studies remains a

question for global implication. However, these studies remain implies in the Asian population in the Asia Pacific region.

Conclusion

This study shows the familial history of CRC, males, metabolic syndrome and smoking were the significant risk factors for CRC in young adult. Modifiable risk factors such as metabolic syndrome and current smoker are noteworthy for young adults.

Disclosure

Author disclose there was no conflict of interest.

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