

# Obesity as Predictor of Mortality of Colorectal Cancer: an Evidence-based Case Report

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## **ABSTRAK**

**Tujuan:** menentukan semua kematian dan kematian spesifik akibat kanker pada pasien kanker kolorektal dengan obesitas. **Metode:** pencarian literatur dilakukan pada Pubmed, Proquest, Ebsco, Scopus, dan Cochrane sesuai dengan pertanyaan klinis. Seleksi judul dan abstrak berdasarkan kriteria inklusi dan eksklusif, filter dobel, pembacaan jurnal secara penuh menghasilkan satu artikel. Studi ini yang berupa metaanalisis dinilai kualitasnya berdasarkan validitas, kepentingan, dan aplikabilitas. **Hasil:** pasien kanker kolorektal dengan obesitas mempunyai risiko relatif untuk mengalami kematian dan kematian spesifik akibat kanker, dibandingkan dengan pasien kanker kolorektal tanpa obesitas. **Kesimpulan:** obesitas berhubungan dengan peningkatan risiko dari semua kematian dan kematian spesifik akibat kanker pada pasien kanker kolorektal. Kontrol dari berat badan sangat direkomendasikan pada pasien ini melalui kombinasi dari diet, aktivitas fisik, terapi perilaku, farmakoterapi, dan bedah.

**Kata kunci:** kanker kolorektal, kematian spesifik akibat kanker, obesitas pradiagnosis, semua kematian.

## **ABSTRACT**

**Aim:** to determine all-cause mortality and cancer-specific mortality of colorectal cancer patient with obesity. **Methods:** a search was conducted on Pubmed, Proquest, Ebsco, Scopus, and Cochrane based on clinical query. The screening of title and abstract using inclusion and exclusion criteria, filtering double, and reading full text led to one useful article. This study, which is meta-analysis was critically appraised for its validity, importance and applicability. **Results:** the relative risk of colorectal cancer patient with pre-existing obesity having cancer-specific mortality and all-cause mortality is 1.22 (95% CI, 1.003-1.35) and 1.25 CI (95% CI, 1.14-1.3) respectively, when compared with non-obese colorectal cancer patient. **Conclusion:** pre-existing obesity is related to increased risk of all-cause mortality and cancer-specific mortality of in colorectal patient. Control of body weight is recommended in this patient through combination of diet, physical activity, behavior therapy, pharmacotherapy, and surgery.

**Keywords:** all-cause mortality, cancer-specific mortality, colorectal cancer, pre-existing obesity.

## INTRODUCTION

Colorectal cancer is the third most common cancer in the world. In Indonesia, age-standardized incidence rates of colorectal cancer are 19.1 for men and 15.6 for women per 100,000 population. Undeniably, the number of colorectal cancer cases is high because Indonesia has more than 250 million populations.<sup>1</sup>

Risk factor of colorectal cancer is multifactorial, one of which is obesity.<sup>2</sup> In Indonesia, prevalence of obesity has increased for every age group.<sup>3</sup> In addition, obesity as a major risk factor, has caused mortality and morbidity for degenerative disease such as cardiovascular disease, dyslipidemia or type 2 diabetes.<sup>4</sup>

Although colorectal cancer patients' survival has improved in last decades, little is known about the prognostic factors which influence survival in colorectal cancer patients.<sup>5</sup> The aim of this evidence-based case report (EBCR) is to critically analyze the impact of pre-existing obesity on both all-cause mortality and cancer-specific mortality in colorectal cancer patients.

## CLINICAL QUESTION

A-52 years old women admitted to hospital with hematochezia since two days prior to admission. She also felt pain, cramp, and abdominal discomfort during defecation since six months ago which are worsen recently. There are history of alternating diarrhea and constipation since four months ago which leads to ten kilograms weight loss in four months. In addition, she easily feel tired. Last week, doctor has diagnosed her having colorectal cancer.

Patient works as an employee in private enterprise for 25 years from 8 AM until 3 PM everyday. She has four children and now lives with her two children who are still in junior high school and senior high school. Her husband passed away ten years ago by a car accident.

Patient's height is 155 centimeters. Patient's weight six months ago was 85 kilograms.

How are all-cause mortality and cancer-specific mortality of colorectal cancer patient with obesity?

## METHODS

A search of literatures was done in December 2nd, 2015 on 5 journal databases including Pubmed, Proquest, EBSCO, Scopus, and Cochrane using terminology listed on **Table 1**. The results obtained from 5 sites were screened by title and abstracts using inclusion and exclusion criteria, filtered double, and checked for those full text availability. After had read full text of those articles, we chose the suitable article for the our EBCR. Critical appraising the meta-analysis study was done by consensus of all authors using guidance for prognosis study from Center of Evidence-Based Medicine.

## RESULTS

We have 10 articles that are suitable for EBCR. After reading the full text, we finally obtained one meta-analysis study. The other 9 articles were already included in this meta-analysis study.

Meta-analysis from cohort studies done by done by Lee et al (2015).<sup>6</sup> The result of critical appraisal of the meta-analysis is shown on **Table 2**. We conclude that the meta-analysis study is valid, important, and relevant to our patient with level of evidence 1a.

This meta-analysis study is aimed to determine association between pre- and post-diagnostic body mass index (BMI) with colorectal cancer-specific mortality and all-cause mortality. It was from Medline and EMBASE database that published between 1970 and September 2014.

## DISCUSSION

We appraised this meta-analysis for its validity, importance, and applicability. Several reasons support validity of this study. This study addresses focused question, selects paper with inclusion criteria, appraises included study, and has similarity from study to study.

In addition, we found that this study is important. The relative risk of patient with pre-existing obesity having cancer-specific mortality is 1.22 with a confidence interval (CI) of 1.003-1.35. Meanwhile, relative risk for all-cause

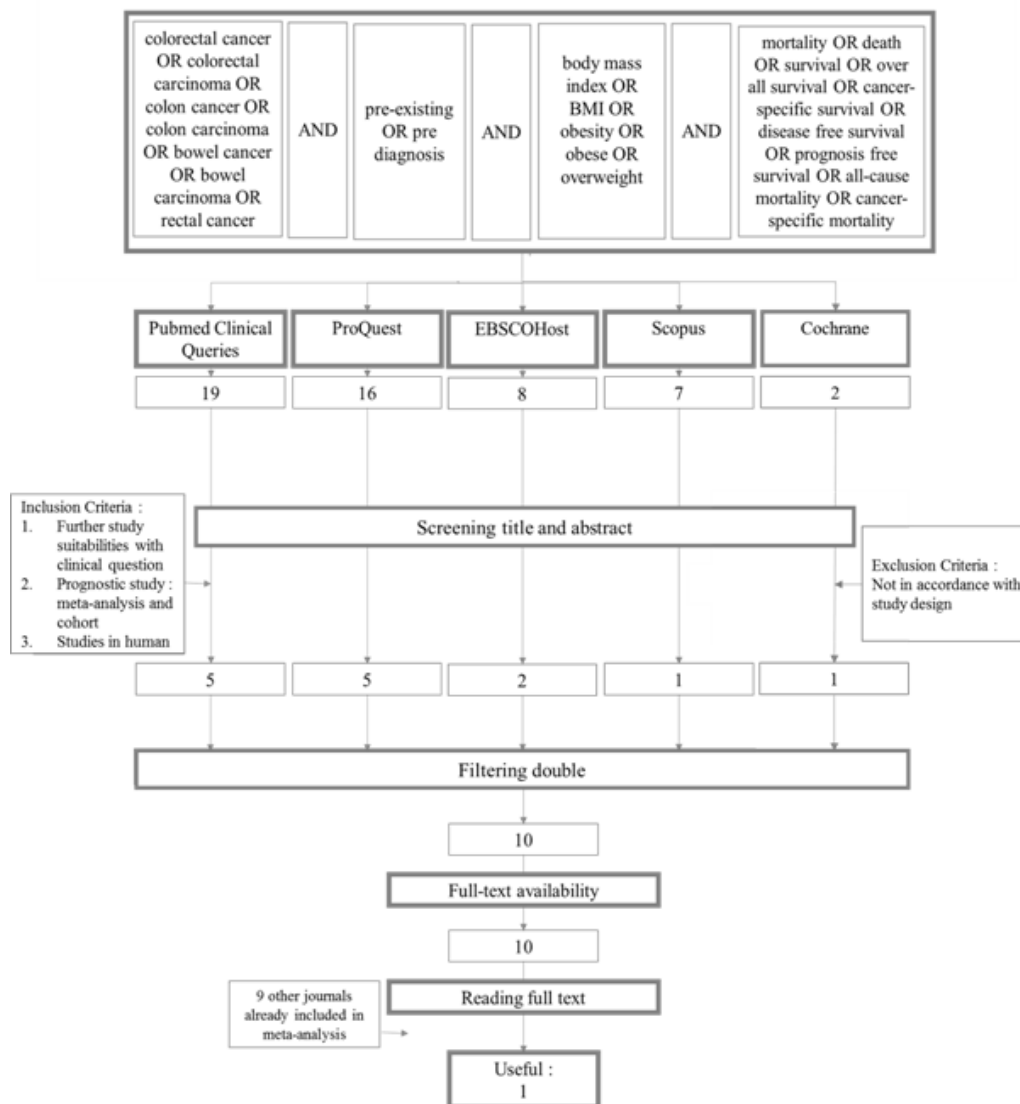


Figure 1. Flowchart of search strategy

mortality is 1.25 with a CI of 1.14-1.36. We can conclude that the value is precise.

This result seems biological-plausible. Although the mechanism of increased mortality in obese patients remain unclear, there are several studies which already able to synthesize possible mechanisms involved. These mechanisms mainly associated with obesity-related hormones, growth factors, modulation of energy balance and calorie restriction, multiple signaling pathways, and inflammatory processes.<sup>7</sup> Goodwin et al. also elucidated about both direct and indirect effect of obesity-associated metabolic and adipose tissue changes and their role on cancer's progression.<sup>8</sup>

Considering this significant role of obesity in colorectal cancer patients' prognosis, we recommended that in order to minimize the consequences of deteriorating prognosis, obesity's management should be applied to all individuals with risk factor of colorectal cancer, such as family history, smoking, dietary intake (low fibre, high intake of red and processed meat), and lifestyle.<sup>9</sup> According to NHLBI guidelines,<sup>10</sup> there are multiple strategies comprised in the effective weight control, including dietary therapy, physical activity, behavioral therapy, pharmacotherapy, and surgery in addition to combination of these strategies.

**Table 1.** Terminology used in 5 journal databases

Location	Terminology	Hits	Selected
Pubmed	Prognosis/Broad [Filter] AND (colorectal cancer OR colorectal carcinoma OR colon cancer OR colon carcinoma OR bowel cancer OR bowel carcinoma OR rectal cancer) AND ((pre-existing OR pre diagnosis) AND (body mass index OR BMI OR obesity OR obese OR overweight)) AND (mortality OR death OR survival OR over all survival OR cancer-specific survival OR disease free survival OR prognosis free survival OR all-cause mortality OR cancer-specific mortality)	19	1
ProQuest	(MESH.EXACT("Sigmoid Neoplasms") OR MESH.EXACT("Anal Gland Neoplasms") OR MESH.EXACT("Colonic Neoplasms") OR MESH.EXACT("Rectal Neoplasms") OR MESH.EXACT("Adenomatous Polyposis Coli") OR MESH.EXACT("Gardner Syndrome") OR MESH.EXACT("Anus Neoplasms") OR MESH.EXACT("Colorectal Neoplasms, Hereditary Nonpolyposis") OR MESH.EXACT("Colorectal Neoplasms")) AND (MESH.EXACT("Body Mass Index") OR MESH.EXACT("Anthropometry") OR MESH.EXACT("Body Weights and Measures")) AND MESH.EXACT("Mortality")	16	0
EBSCOHost	(colorectal cancer OR colorectal carcinoma OR colon cancer OR colon carcinoma OR bowel cancer OR bowel carcinoma OR rectal cancer) AND ((pre-existing OR pre diagnosis) AND (body mass index OR BMI OR obesity OR obese OR overweight)) AND (mortality OR death OR survival OR over all survival OR cancer-specific survival OR disease free survival OR prognosis free survival OR all-cause mortality OR cancer-specific mortality)	8	0
Scopus	TITLE-ABS-KEY (colorectal cancer OR colorectal carcinoma OR colon cancer OR colon carcinoma OR bowel cancer OR bowel carcinoma OR rectal cancer) AND TITLE-ABS-KEY (body mass INDEX OR bmi OR obesity OR obese OR overweight) AND TITLE-ABS-KEY (mortality OR death OR survival OR over ALL survival OR cancer-specific survival OR disease free survival OR prognosis free survival OR all-cause mortality OR cancer-specific mortality) AND SUBJAREA (mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal)	7	0
Cochrane	(colorectal cancer OR colorectal carcinoma OR colon cancer OR colon carcinoma OR bowel cancer OR bowel carcinoma OR rectal cancer) AND ((pre-existing OR pre diagnosis) AND (body mass index OR BMI OR obesity OR obese OR overweight)) AND (mortality OR death OR survival OR over all survival OR cancer-specific survival OR disease free survival OR prognosis free survival OR all-cause mortality OR cancer-specific mortality)	2	0

**Table 2.** Critical appraisal of meta-analysis<sup>6</sup>

	Did the meta-analysis address a focused question?	Yes
	Were the criteria used to select articles for inclusion appropriate?	Yes
Validity	Is it likely that important relevant studies were missed?	No
	Was the validity of the included studies appraised?	Yes
	Were the assessments of studies reproducible?	Yes
	Were the results similar from study to study?	Yes
Importancy	What are the overall results of the meta-analysis?	Pre-existing obesity was associated with increased colorectal cancer-specific mortality (RR: 1.22, 95% CI: 1.003–1.35, p<0.01) and all-cause mortality (RR: 1.25, 95% CI: 1.14–1.36, p<0.01)
	How precise were the results?	Precise, 95% CI interval for colorectal cancer-specific mortality and all-cause mortality is narrow
Applicability	Can the results be applied to my patient care?	Yes
	Were all clinically important outcomes considered?	Yes
	Are the benefits worth the harm and costs?	Yes

As for our patients, with BMI 35.37 kg/cm<sup>2</sup> before the colorectal cancer diagnosis, the strategies recommendation is combination of diet, physical activity, behavior therapy, and pharmacotherapy. Based on National Institutes of Health,<sup>10</sup> we have to conduct dietary assessment first in order to determine the baseline of eating pattern and select the optimal intervention. The dietary intake recommended with BMI of 35.37 kg/cm<sup>2</sup> on 52-year old woman with moderate activity is 1800 calories/day. Physical activities recommended include swimming, jogging, dancing, or cycling.

### CONCLUSION

Pre-existing obesity is related to increased risk of all-cause mortality and cancer-specific mortality of in colorectal patient. Control of body weight is recommended in individuals with risk factors before diagnosis of colorectal cancer. The recommendation of weight control strategies for this patient before the colorectal cancer diagnosis is combination of diet, physical activity, behavior therapy, and pharmacotherapy

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