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RESEARCH ARTICLE

Relationship Between Family History, Bloody Stool, Palpable Mass, Anemia and MSCT Abdomen and Kolon Carsinoma Cross-Sectional Study at Dr.Kariadi General Hospital in 2016

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ABSTRACT

Background: *Colon cancer, a colorectal cancer, is the third most common epithelial malignancy in the world. Family history, bloody stool, palpable mass, anemia, and abdominal MSCT are symptoms and signs of colon carcinoma.* ***Objective:*** *To determine the relationship between the 5 variables and the incidence of colon carcinoma at Dr. Kariadi Hospital, Semarang in 2016.*

Methods: *a Cross-sectional observational analytical study using medical record (RM) and complementary primary data. The inclusion criteria were the complete medical record, and clinical diagnosis of suspected colon carcinoma. Data obtained from the department of Anatomy Pathology/PA (11,794 PA results) were traced to the medical record section (46 patients with suspected colon carcinoma). The incomplete data were confirmed by: contacting the patient/family, obtaining the archive in the laboratory and radiology resulting in 27 patients meeting the inclusion criteria. Analysis was done using chi-square test, Spearman-Kendall bivariate correlation, and logistic regression.*

Results: *Abdominal MSCT was moderately associated with colon carcinoma ($p = 0.003$; $r = 0.488$), while family history, bloody stool, palpable mass, and anemia were not associated with colon cancer. Analysis between predictors of outcome: Bloody stool was moderately associated with anemia ($p = 0.006$; $r = 0.411$), and anemia was weakly associated MSCT ($p = 0.035$; $r = 0.351$). Abdominal MSCT was the predictive factor for colon carcinoma ($p = 0.021$).*

Conclusion: *Abdominal MSCT was found to be associated with the incidence of colon carcinoma. Bloody stool was associated with anemia, and anemia was associated with abdominal MSCT. MSCT was the predictive factor for colon cancer.*

Keywords: *predictors, diagnosis, family history, bloody stool, palpable mass, anemia, MSCT abdomen, colon carcinoma*

BACKGROUND

Cancer is one of the main causes of morbidity and mortality worldwide. In 2012, around 14 million new cases and 8.2 million deaths occurred due to cancer and are predicted to increase by 22 million cases in the next two decades(World Cancer Report, 2015). In Indonesia, data from the Ministry of Health (2007) shows that cancer ranked fourth causes of death from non-infectious diseases, after heart attacks, strokes, and diabetes mellitus. The increasing incidence of cancer is due to the high number of new cases of cancer that come at an advanced stage (Kemenkes RI, 2015) Colorectal cancer is the third most common epithelial malignancy in the world. Every year there are around 1,000,000 new cases and 500,000 deaths from colorectal cancer (Tanaka et al., 2010). In Indonesia, in 2008, the incidence of colorectal cancer was 15.6 per 100,000 female population and 19.1 per 100,000 male population(World Health Organisation, 2011). In Semarang there were 160 cases of colorectal carcinoma in 2010, of which 35% were aged 51-60 years (Parish et al., 2011). The limited funds (including insurance) and infrastructure for diagnostic testing in hospitals/ health services in the regions (including rural areas) are part of the reason for the need for a new diagnostic method consisting of a combination of history, physical examination, and minimal supporting examinations that can predict colon carcinoma events effectively and efficiently.

Determination of the type of disease by

determining the diagnosis is absolutely necessary for the management of appropriate treatment. Incorrect diagnosis can lead to a series of errors that can lead to the loss of the patient and family (Sastroasmoro and Ismoel, 2014)(Sastroasmoro and Ismoel, 2014). Increased access to diagnostic services makes more cancer patients can be diagnosed at an early stage (Biswas, Ades and Hamilton, 2015). There has been a large body of evidence about the predictive value of cancer symptoms from retrospective studies (Esteva et al., 2013), but the quality of recorded data was limited (Walter et al., 2016). Thus, in recent years, mortality rates due to colonic carcinoma have increased in many developing countries (Haggar, Boushey and Ph, 2009).

After a good history taking and physical examination, laboratory examination data and other supports can help establish the diagnosis (Simatupang, 2010). Until now, there have been no studies examining a mixture of various variables consisting of history, physical examination, and investigations to predict the incidence of colon carcinoma. On history taking, data from family history and bloody stool were chosen because meta-analyzes and systematic reviews showed that both have been more predictive as the risk of colon carcinoma than complaints of fatigue, nausea, fever, decreased appetite, weight loss, abdominal pain, changes in bowel habits, flatulence, peri-anal symptoms and tenesmus (Boardman et al., 2007; World Cancer Research Fund and American Institute for Cancer Research, 2007; Jellema et al., 2010; Etzel et al., 2012; Astin et al., 2014; Park et al., 2014; Jensen et al., 2015). On physical examination, data from abdominal palpable mass was chosen because many studies showed that patients with abdominal palpable mass, especially in a large size has a greater likelihood of colon carcinoma (Ang et al., 2008; Sjamsuhidajat R (ed), de Jong (ed), Karnadiharjo W (ed), Prasetyono TOH (ed), 2011; Vega-Villaamil et al., 2013; Park et al., 2014; Kato et al., 2016; Renzi et al., 2016). On laboratory investigation, the presence of anemia, was selected as the risk factor because many systematic studies and reviews suggesting that anemia increases the likelihood of colon carcinoma with a high specificity and all hospitals can do it. (Ludwig et al., 2004; Spivak, Gascon and Ludwig, 2009; Bekkink et al., 2010; Tettamanti et al., 2010; Macciò et al., 2014). On radiological investigations, abdominal CT (abdominal MSCT) was selected as risk factor because literature, guidelines, systematic review and meta-analysis recommended abdominal CT for colorectal carcinoma (National Institute for Health and Care Excellence (NICE) Guideline, 2014; Taylor CR, Lin EC, 2015; Nerad et al., 2016; Teama, El-Badry and Yousef, 2016) In addition, CT scan can determine tumor location, tumor size, staging of colon cancer before surgery, assessing and staging recurrent disease, detecting distant metastases, providing high diagnostic accuracy and information about secondary tumors, differentiating between benign and malignant neoplasms. In addition, many regional hospitals can do it.

New methods capable of diagnosing colon cancer at early stage are needed to reduce mortality due to late diagnosis. Before carrying out a new diagnostic test on a larger samples, it is necessary to conduct a study to find a relationship between family history, bloody stool, palpable mass, anemia, and abdominal MSCT and the incidence of colon carcinoma in Dr.Kariadi Hospital Semarang in 2016.

METHODS

This type of research was observational analytical study with a cross-sectional design. The samples was all cases of colonic carcinoma in Dr.Kariadi General Hospital Semarang in 2016 as many as eligible 46 patients. The inclusion criteria were complete medical record data (RM) with clinical diagnosis of suspected suspect colon carcinoma. Exclusion criteria were site of PA biopsy sampling were not in colon (i.e. the intestine, ileocaecal, ileum to certain colon, rectosigmoid, colorectal, rectum, or anus); undergoing chemotherapy; or taking long-term analgesic/steroid drugs.

The consecutive sampling method was used on secondary data from RM during 2016, supplemented with primary data for validation by contacting the patient/family. Data collection was carried out at Dr. Kariadi Semarang in July - October 2017.

Data collection was carried out in the Anatomy Pathology section followed by recording the identities of all patients whose biopsy samples were sent to Pathology Anatomy with suspicion of colon carcinoma (suspect colon carcinoma, colon mass, intra-abdominal tumor, ileus obstruction, hematoschezia, hematemesis, melena, anemia, fever, or constipation). The number of positive and negative carcinoma cases from the data was recorded. Data retrieval continued to the RM section looking for patient documents according to the identity obtained. Family history data, bloody stool, and palpable mass confirmed/verified by contacting the family via WhatsApp application (WA)/Short Messaging Services (SMS)/telephone whose number is written in RM. If the family cannot be contacted, then the data in the RM was used. Anemic data is obtained from RM, but if the RM is unclear, it is verified by

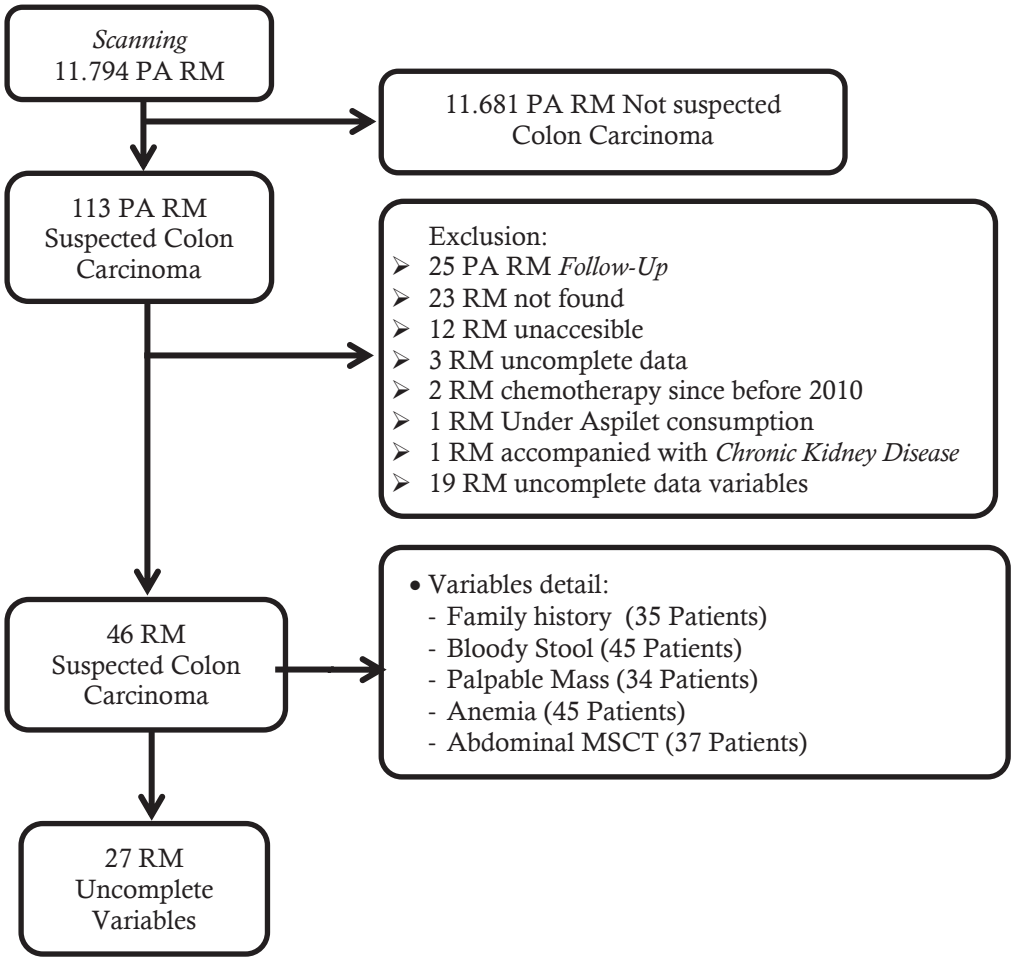

Figure 1. Consort of Research Results

acessing the archive at the laboratory installation. CT-scan data was obtained from RM, if it is incomplete/ unclear then the data were obtained by searching the archive at the radiology installation.

After obtaining validated data from 46 patients, there were 27 patients with complete data (Figure 1). This research was conducted after ethical clearance approval from the Health Research Ethics Commission (KEPK) of the Medical Faculty of Diponegoro University and Dr. Kariadi Hospital Semarang.

STATISTICAL ANALYSIS

To determine the relationship between each variable and the incidence of colon carcinoma and the relationship among the variables themselves, chi-square analysis was used. All chi-square results showing correlation then analyzed for correlation by Spearman-Kendall bivariate correlation analysis to determine the strength of the relationship. To determine the variables that have the strongest relationship with colon carcinoma, regression analysis was conducted. All statistical analysis was carried out using the SPSS 21 application.

RESULTS

Patients included in this study were 35 patients for family history variables, 45 patients with bloody stool, 34 patients with palpable mass, 45 patients for anemia, and 37 patients for MSCT abdomen. There were 27 patients with the complete data including family history, bloody stool, palpable mass, anemia, and abdominal MSCT (table 1).

After observing the five variables, it was found that the history of colon carcinoma in families up to 2 generations above (siblings, parents, siblings of parents, grandparents) was only found in 1 patient with colon carcinoma. Blood history in faeces (bloody stool) is found in 13 patients with colon carcinoma. The palpable abdominal mass was present in 15 patients with colon carcinoma. Symptoms of anemia occur in 29 patients with colon carcinoma. The description of abdominal MSCT suggestive of colon carcinoma was found in 22 patients with colon carcinoma (Table 2).

Table 1. Baseline data of Patients with family history, bloody stool, palpable mass, anemia, and abdominal MSCT

Characteristics	Frequency (%)
Sexes	
• Male	30 (65.22)
• Female	16 (34.78)
Ages	
• <40 years	6 (13.04)
• 40-49 years	9 (19.57)
• 50-59 years	18 (39.13)
• 60-69 years	9 (19.57)
• ≥70 years	4 (8.70)
Ability to Contact the Patient/Family	
• Reachable	32 (69.57)
• Unreachable	14 (30.43)
Patient's Recent Condition*	
• Alive	19 (41.30)
• Dead	23 (50)
• Unknown (No contact)	4 (8.70)

Table 2. Relationships between Variables (family history, bloody stool, palpable mass, anemia, and abdominal MSCT) with Occurrence of Colonic Carcinoma

		Colon Carcinoma (+)	Colon Carcinoma (-)	TOTAL	*P**	R**
Family History	(+)	1	1	**35**	**0.630**	**-**
	(-)	22	11			
Bloody Stool	(+)	13	6	**45**	**0.734**	**-**
	(-)	19	7			
Palpable Mass	(+)	15	5	**34**	**0.273**	**-**
	(-)	8	6			
Anemia	(+)	29	8	**45**	**0.100**	**-**
	(-)	4	4			
Abdominal MSCT	(+)	22	3	**37**	**0.003**	**0.488**
	(-)	5	7			

***Correlation test with Chi-square, significant only if p<0.05**

****Power or correlation with Spearman-Kendall bivariate correlation test, significant only if p<0.05**

Tabel 3. Inter variables correlation (family history, bloody stool, palpable mass, anemia, and abdominal MSCT) on Colon Carcinoma Occurence

No.	Nama Prediktor – Prediktor Lain pada Kejadian Karsinoma Kolon	*P**	R**
1.	Riwayat Keluarga – *Bloody Stool*	0,766	-
2.	Riwayat Keluarga – *Palpable Mass*	0,198	-
3.	Riwayat Keluarga – Anemia	0,289	-
4.	Riwayat Keluarga – *MSCT Abdomen*	0,657	-
5.	*Bloody Stool – Palpable Mass*	0,238	-
6.	*Bloody Stool* – Anemia	**0,006**	**0,411**
7.	*Bloody Stool – MSCT Abdomen*	0,536	-
8.	*Palpable Mass* – Anemia	0,279	-
9.	*Palpable Mass – MSCT Abdomen*	0,216	-
10.	Anemia – *MSCT Abdomen*	**0,035**	**0,351**

The results of chi-square analysis showed that there were no significant relationships between 4 variables (family history, bloody stool, palpable mass, and anemia) and colonic carcinoma, p> 0.05. In contrast, there was a moderate relationship between abdominal MSCT and the incidence of colon carcinoma (p<0.05, R = 0.488).

To determine the relationship between variables among 5 variables (family history, bloody stool, palpable mass, anemia, and abdominal MSCT) in the incidence

of colonic carcinoma, chi-square test was performed and continued with Spearman-Kendall correlation test if there was a relationship. The results of the analysis showed that bloody stool was moderately associated with anemia ($p<0.006$, $R = 0.411$). Likewise with anemia variables was weakly associated with abdominal MSCT ($p<0.05$, $R = 0.351$). While the other variables did not have a significant relationship ($p> 0.05$) (Table 3).

DISCUSSION

The results of this study indicate that family history factors have no relationship with colonic carcinoma. This finding supports a study showing that there were no differences in clinical pathological characteristics or prognosis of patients with or without a family history of hepatocellular carcinoma (Huang J et al., 2013). In addition, a systematic review of 6 articles of prostate cancer stated that a family history of prostate cancer does not increase the risk of progression from prostate cancer (Telang et al., 2017). According to Haggar and Boushey, the reason for the increased risk is still unclear, but may be due to genetic, environmental factors or a combination of both, (Haggar, Boushey and Ph, 2009). On the other hand, the study reported by Boardman et al showed that patients with a history of colorectal cancer or adenomatous polyps in one or more than one of first-degree relatives (parents, brothers, sisters or children (National Cancer Institute, 2016) have an increased risk of malignancy (Boardman et al., 2007). The risk will be higher in patients with a family history of colorectal cancer or adenomatous polyps at any first-degree relatives aged <60 years, or a history of colorectal cancer or adenomatous polyps in 2 or more first-degree relatives of any age (Boardman et al., 2007). In this present, due to the small number of samples and the family history of colon carcinoma of the Indonesian population is not as many as the other country population, there is no relationship between family history and colon carcinoma In addition, the symptoms/signs of colon cancer with the identified mass in the stomach were found in a small number of patients (0.2% of cases) (Park et al., 2014) causing no relationship between family history and the palpable mass.

The bloody stool factor was not associated with colon carcinoma. This is in line with previous study finding showing that suspected source of bleeding originated from 5 mm polyps, hemorrhoids, or right-sided diverticula, where the study was entirely carried out at only one center with a very small sample size (range 10-53), and carried out more than 15 years ago with the poor quality of endoscopic imaging in colonoscopy(Etzel et al., 2012). Etzel et al study also suggested that colon tumors were found in about 1.7% of the melena population (Etzel et al., 2012), which is a small number. This is not in line with the research of Park et al who stated that in symptomatic right colon carcinoma patients there were 20.9% of blood stool symptoms, whereas symptomatic left colon carcinoma showed more blood stools at 35.2% (Park et al., 2014). Inconsistent results in this study could be due to the small number of samples obtained by researchers as in Etzel's study (Etzel et al., 2012), so the bloody stool is not related to colon carcinoma.

The palpable mass factor has no relationship with colonic carcinoma. This is in line with the American Cancer Society which states that not all masses are cancer. The fact is most tumors not cancer (american Cancer Society, 2015). Park study found that symptoms/signs of colon cancer with the discovery of abdominal mass were very few, which is only 0.2% of cases (Park et al., 2014). This is because small tumors at an early stage are not palpable in the abdominal palpation, and the tumor is exposed to the condition. Mass in the sigmoid is more palpable than mass in other parts of the colon (Sjamsuhidajat R (ed), de Jong (ed), Karnadiharjo W (ed), Prasetyono TOH (ed), 2011). This finding is not in line with the rest of the American Cancer Society's claim that the mass that can be cancer can be found to feel like a mass during a physical examination (american Cancer Society, 2015).

Anemia had no relationship with colon carcinoma. This is in line with Maccio et al who stated that anemia in oncology patients is often regarded as a side effect of cancer therapy (Macciò et al., 2014). There was positive correlation between hepcidin and Hb levels, in which low hepcidin levels are initially predictive for severe anemia (Durigova et al., 2013). The emergence of iron deficiency anemia with anemia in chronic diseases together often occurs in the elderly and patients with chronic kidney disease (Camaschella and DL, 2015). This is not in line with research which states that mild anemia is significantly associated with cancer diagnosis (Tettamanti et al., 2010). More than 30% of cancer patients have anemia at the time of diagnosis, where the lowest hemoglobin level is found in advanced cancer patients (Macciò et al., 2014). Research by Shu et al. concluded that anemia in cancer patients, who are chronic, has hepcidin levels that are positively correlated with IL-6 and in contrast to serum iron (Shu et al., 2015). Different results in this study can be caused also because the number of samples obtained is still insufficient, so statistically there was no relationship between anemia

and carcinoma of the colon.

Abdominal MSCT factor is associated with colon carcinoma and has moderate relationship strength, and is a variable that can be used to predict the occurrence of colon carcinoma. This is in line with Nerad's study in the form of a systematic review and meta-analysis that took data from 13 CT-scan studies, concluding that CT scans have good sensitivity to detect T3-T4 tumors (sensitivity 90% and specificity 69%), although has low accuracy for detecting node involvement (Nerad et al., 2016). This study was also supported by studies conducted by Taylor et al who stated that CT-scans (including multi detector computed tomography (MDCT) and CT-colonography can be used as additional screening for colon carcinoma, determining tumor location, tumor size, as colon cancer staging before surgery, to assess and staging recurrent disease, and detect the presence of distant metastases. In addition, CT scans can also be used to confirm the diagnosis of incidental/ accidental colon tumors in suspicion of other diseases (Taylor CR, Lin EC, 2015) because MSCT provides high diagnostic accuracy in the detection of tumors and staging to lymph node metastases, and has high reliable information on secondary tumors. Moreover, MSCT provides advantages in imaging, where intravenous contrast enhancement improves the accuracy of carcinoma evaluation (Teama, El-Badry and Yousef, 2016). This is not in line with systematic reviews and a meta-analysis of 25 studies on the diagnostic modalities of colorectal cancer metastases to the liver, the results were that MRI was superior to CT-scans, where CT scans sensitivity 4.8% and its specificity is 95.6%, while MRI sensitivity is 81.1% and its specificity is 97.2%, so it is still better for MRI than CT-scan (OR = 0.69). It was also compared with FDG-PET examination which had a successive sensitivity and specificity of 93.8% and 98.7% (Floriani et al., 2010). In addition, Kang B et al's study, which results in PET/MRI integrated throughout the body, adds value to Contrast-Enhanced CT (CECT) in detecting metastatic lesions and unclear characterization of lesions, suggesting that PET / MRI can help select appropriate treatment strategies for patients with colorectal cancer (Kang et al., 2016).

The bloody stool and anemia factors were moderately associated with colon cancer. This is in accordance with Arisman's research stating that iron deficiency anemia is generally caused by three things, namely chronic blood loss, iron intake and inadequate absorption, and increased iron requirements. Chronic blood loss for example in malignancy process (Arisman, 2010). In this case anemia is more closely associated with chronic bleeding due to colorectal cancer than as a cause of cancer of the colon itself. This is supported by the results of statistical analysis that illustrates that anemia and abdominal MSCT have low relationship strength.The results of this study indicates that among the 5 symptoms and signs of colonic carcinoma variables only abdominal MSCT was associated, while other variables were not related to colonic carcinoma.

Limitations of this study include: (1) Age of selected patients was not limited, which may affect the status of immunity; (2) the latest intelligence/education level of the patient and the patient's family, which can affect the patient's/family's memory history so that recall bias can occur; (3) Mortality, whereby to complete the data with primary data must contact the family of patients who do not necessarily represent the actual condition of the patient, and the patient's family was not willing to collect the data on the deceased patient; (4) Medical record data: (a) Many are incomplete, where physical and supporting examinations were not always carried out and written in medical record (only taken by patients); (b) Missing contact/no telephone number to contact; (c) medical record data access was limited; (5) Research time was only 1 year (January - December 2016); and (6) Location, only conducted in one research center.

Referring to these limitations, further research needs to increase the number of samples from several hospitals/multicenter with a cohort study design for at least 2 years, continuing this study with discriminant analysis and as a new diagnostic test with composite variables, as well as adding predictor variables such as abdominal pain.

CONCLUSION

In general, it can be concluded that there was a relationship between abdominal MSCT and colon carcinoma, while family history, bloody stool, palpable mass, and anemia were not associated with the colonic carcinoma. Thus, abdominal MSCT can be suggested to be a predictive factor for colon carcinoma.

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