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Review

Colorectal cancer and potential predictors of never screened for faecal occult blood test: A narrative review

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Abstract

Colorectal cancer (CRC) is a major public health threat. Therefore, CRC screening uptake has been a focus with the established precancerous lesion and the strong association of early detection with staging and survival of the disease. However, CRC screening is relatively low in many countries. This article briefly discussed the current situation of CRC, recommendations, and current uptake of CRC screening in various countries. Besides that, this article also highlights the potential factors that help to predict the CRC screening uptake worldwide. Identification of those factors could guide policymakers to develop an effective strategy to improve the CRC screening uptake and ultimately improve the health outcome of the population.

Introduction

Colorectal cancer (CRC) is one of the most common cancers in Asia and worldwide with an estimation of 10.9% of cancer death among men and 9.5% among women.[1] Mortality and morbidity associated with CRC are highly preventable with early diagnosis and treatment. Most of the CRC cases appear to develop from benign and precancerous polyps in which the incidence and mortality can be reduced by performing early screening through the removal of adenomatous polyps and sessile serrated polyps.[2] Therefore, it is vital to ensure that the uptake of CRC screening reaches the optimal level to reduce the overall CRC incidence and mortality. Previous studies reported that various factors influence the public's decision to avoid FOBT screening including sociodemographic and socioeconomic background,[3,4] health access factor,[5,6] preventive behaviour,[7] as well as knowledge and attitude regarding CRC.[8-12] This review will briefly discuss the current situation of CRC, recommendations for CRC screening, and how various factors could affect the uptake of CRC screening.

Global situation of colorectal cancer

In 2018, the International Agency for Research on Cancer (IARC) estimated that 18.1 million new cases and 9.6 million deaths were related to CRC. CRC was ranked as the third most common malignancy worldwide, and the third leading cause of cancer detected in men and women. Moreover, CRC is also second-highest cancer related to death after lung cancer worldwide.[1] The overall CRC trends of incidence and mortality vary between countries with an increasing trend was observed in low- and middle-income countries while a more stabilised and decreasing trend was observed in high-income countries.[13] The decrease in CRC mortality can be partly explained by improved survival of CRC patients through the adoption of best practices of cancer management and treatment, early detection efforts, and removal of polyps. The introduction of screening methods might initially cause an increase in the incidence of CRC. However, in a long term, it has been shown to reduce the incidence of CRC by the removal of precancerous polyps *via* colonoscopy.[14] An increase in risk factors such as physical inactivity, cigarette smoking, obesity, and low fibre diet have been associated with the increasing trend of CRC prevalence especially in low- and middle- income countries.[15]

Significance for public health

This study highlights the public health challenge in early screening for colorectal cancer (CRC). The prevalence of never screened for faecal occult blood test is relatively high. This review dissects the issue and further discuss on the predictors, which could guide policymakers in developing strategy to improve CRC screening uptake.

CRC situation in South East Asia and Malaysia

The GLOBOCAN project reported that Malaysia has the third-highest overall incidence (18.3 per 100,000 population) of CRC in South East Asia (SEA) after Singapore (33.7 per 100,000) and Brunei (25.0 per 100,000).[1] Most SEA countries experiencing a rise in CRC due to an increase in lifestyle-related risk factors such as unhealthy dietary intake, physical inactivity, and obesity.

According to Malaysian National Cancer Registry, CRC is the second most common cancer (13.5% from all type of cancer) after breast cancer (19.0%) among the Malaysian population. It was reported that a total of 15,515 CRC cases were registered from 2012 to 2016. About gender, majority of CRC cases were reported among males (56.1%) compared to females (43.9%). The lifetime risk of CRC among males was 1 in 55 (cumulative risk 1.8) while female reported a ratio of 1 in 77 (cumulative risk 1.3). CRC was also observed to be the most common cancer among males (ASR 14.8) and the second most common among females (ASR 11.1) after breast cancer. The lifetime risk among Chinese males was the highest (1 in 43) followed by Malay males (1 in 65), and Indian males (1 in 70). A similar trend was also observed in females whereby the lifetime risk was highest among Chinese (1 in 57) followed by Malay (1 in 89) and Indian (1 in 95). According to a report, CRC incidence increased with age and peaked at the age of 70 and above for both sexes.[16]

Staging of CRC at the time of diagnosis for males was 7.4% at stage I, 20.2% at stage II, 32.8% at stage III, and 39.6% at stage IV. Meanwhile, in females, the staging at the time of diagnosis was only 6.6% at stage I, 20.3% at stage II, 32.9% at stage III, and 40.2% at stage IV. Therefore, at the time of diagnosis, there were 72.4% CRC cases among males and 73.1% CRC cases among females that were already at the advanced cancer stage (stage III and IV).[16-18] It was reported that in 2015, malignant neoplasm has become one of the top five major cause of deaths in the Malaysian government hospital. Most of the CRC cases were detected at the late stage in which more than half of CRC patients were detected at stage III and IV.[17] Meanwhile, another study showed that the median age for CRC was 62 years old with a 65.0 per 100 000 incidence rates among the Chinese. In Sabah, Malaysia, indigenous populations develop CRC at an early age and present themselves at the hospital when the disease is at the advanced stages.[19]

Natural history and adenoma-adenocarcinoma sequence

CRC occurs in the large intestine and rectum whereby it develops on the lining of the large bowel starting from precancerous lesion. The precancerous lesions that commonly progressed into CRC are adenomas or adenomatous polyps. The progression of the precursor lesion of adenomatous polyps into CRC is also known as adenoma-adenocarcinoma sequence.[20] The neoplastic changes initially begin within the epithelium of the bowel lining, which is called intraepithelial neoplasia. This will then progress into cancer with invasion across the basement membrane.[21] The progression of CRC *via* adenoma-adenocarcinoma sequence has also been reported to be via alternative routes of serrated neoplasia pathway. Statistic showed that more than 15% of CRC originated from the serrated neoplasia pathway.[22] The potential of cancer development from the precancerous lesion can also be explained by the size of adenoma with 1% in small polyps (size less than 1 cm), 10% in adenomas (size more than 1 cm and less than 2 cm), and 50% in adenomas (size larger than 2 cm). A study among Malaysian patients who underwent colonoscopy in the government hospital revealed that 58% of polyps morphology was sessile with 5-9mm size and 19.1% adenoma detection rate.[23]

Screening and CRC precancerous lesion

CRC has become the focus of screening due to the established precancerous lesion and the strong association of early detection with staging and survival of the disease. World Health Organization (WHO) has set ten principles for the establishment of screening programmes to detect the disease.[24] It was stipulated that:

1) The condition sought is an important health problem
2) There should be accepted treatment in those with recognised disease
3) Facilities for diagnosis and treatment must be available
4) There should be a recognisable early stage of the disease
5) There should be a suitable test or examination
6) The test is accepted by the population
7) The natural history of the disease must be adequately understood
8) There should be an agreed policy to treat on whom to treat as a patient regarding treatment
9) The cost of diagnosis and treatment must be balanced economically with possible expenditure on medical care
10) The case finding must be a continuing process

CRC screening recommendations

An independent group of experts from the United States Preventive Service Task Force (USPSTF) has recommended CRC screening among the average risk individuals from 50 to 75 years old. The recommended screening tools include Guaiac based FOBT Test (gFOBT) or immunochemical FOBT test (iFOBT) conducted annually, flexible sigmoidoscopy for every 5 years, 10 years of yearly colonoscopy, CT colonography for 5 years every year or combine test of 10 years of yearly flexible sigmoidoscopy with annual iFOBT. These screening recommendations are shared by other countries such as the United Kingdom.[25,26] However, some countries are against colonoscopy as a primary CRC screening tool due to the lack of high-quality evidence, lack of human resources (require gastroenterologist to perform the procedure) with long waiting time for the screening, greater potential for harm, and higher risk of complications.[27] FOBT is favourable in countries with limited colonoscopy resources.[28] Even though single FOBT has low sensitivity to detect CRC,[29,30] many western countries considered FOBT as the best population-based screening. This is due to its simplicity and high acceptance even in countries with the well-developed healthcare system. In a retrospective cohort study among iFOBT screening participants, repeated annual iFOBT was associated with high sensitivity for CRC detection.[31] In a population-based cohort study in Japan, there was a decrease in mortality rate at about 72% among individuals who are screened using iFOBT compared to unscreened subjects. Although the screening method does not significantly reduce the incidence of CRC, it was reported that the screening has been associated with the reduction of the advanced stage of CRC.[32] In Malaysia, the Ministry of Health has recommended selective opportunistic screening among asymptomatic individuals from the age of 50 to 75 years old using guaiac-based or immunochemical-based faecal occult blood test.[33]

Uptake of CRC screening

Participation in screening is one of the key indicators for programme acceptance and effectiveness. Due to the availability of screening and treatment option for CRC, many countries have been promoting faecal testing in asymptomatic individuals with an average risk of CRC development. However, most countries have not achieved the desired level of screening uptake. Recommendation by European Commission states that the minimum uptake of CRC screening among the average risk group is 45% with 65% of optimum rate.[34] The American Cancer Society sets a higher goal for screening uptake in 2018, which is 80% compared to 75% in 2017.[35] Despite the evidence and presence of specific guidelines, the prevalence of populations that have never presented themselves for colorectal screening especially using FOBT varies and is relatively high. An intervention study in health clinics in Israel found that the prevalence of non-screened for FOBT among the control group (no reminder system) was 98.8%.[36] In another intervention study in Canada reported that the non-responder to a mail invitation to perform FOBT at the nearest healthcare facility was as high as 90.4%.[37] Similar findings were also observed in the United States with a 90.1% prevalence of non-compliance to current FOBT screening.[5] Canadian health survey showed 76.5% prevalence of respondents who have never had any history of colorectal cancer screening.[38] Meanwhile, in Asia, several countries have recorded variation in CRC screening uptake. In Japan, the screening program was in place since 1992 with a participation rate of 41.4% in men and 34.5% in women using the Faecal Immunochemical Test (FIT).[39] In South Korea, the CRC screening program using FIT that was implemented in 2004 showed a 10.5% increase participation in 2004 to 21.1% in 2008 and to 25% in 2012.[40] In Thailand, a pilot program that was implemented in 2011 showed 37.1% non-participation for FIT.[41] In Taiwan, the defaulters in the pilot FIT program were found to be high at 78.6%.[42].

However, study on the acceptance of CRC screening in Malaysia is limited. A recent study performed in Sabah, Malaysia recorded a prevalence of 85.8% population that has never been screened by FOBT.[43] Another study among average risk individuals in West Malaysia found that there were only 13 respondents or 0.7% (out of 1905 respondents) that have been screened for CRC.[44] In a multicentre study in the Asia Pacific region, Malaysia recorded among the highest prevalence with poor participation of CRC screening (97%) compared to another country in the same region such as the Philippines (31%), Japan (62%), and Brunei (86.3%).[45] The issue with screening may benefit from smart healthcare delivery to improve access via digital health integration. Screening and referral of cases for further intervention can be done earlier.[46]

Potential predictors of CRC screening uptake

Sociodemographic factors

There were several studies that have addressed the association of age with CRC screening uptake. In a study in England, it was found that older respondents have a significantly higher screening uptake compared to the younger age group (60-64: 62.6% *vs* 65-70:74.3%, p<0.001).[47] This finding is consistent with a study in the United States that found participants within the age group of 65 to 75 years old has 2.49 higher odds at receiving CRC screening compared to those of 50 to 64 years old.[3] This contrasts with a longitudinal cohort study in the US whereby the likelihood of being up to date to screening practices was lower in the older age group (>76 years old) compared to the younger age group (p<0.001). A lower screening uptake among the older age group could be explained by the comorbidity influences in relation to older age.[48] This contrasts with another report whereby the older age group have higher CRC screening uptake, especially in the United States. This is due to a special programme implemented by the US known as National Health Insurance Programme or Medicare that covers health-related expenses including cancer screening for US citizens age 65 years old and above.[3]

Several studies have shown gender inequality in CRC screening uptake. A study in the US showed that the utilisation of FOBT was common among women compared to men (OR=1.8, 95% CI: 1.6-2.0).[5] This is consistent with a pilot study in the United Kingdom on FIT acceptability that showed men have lower acceptance on both guaiac-based FOBT and FIT compared to women.[49] Another study also reported a similar finding whereby women has significantly higher screening uptake using FIT compared to men (women 50.2% *vs* men 54.6%, p<0.001) in a population-based CRC screening program in Barcelona.[50] This is further supported by a meta-analysis study, which stated that male uptake was significantly lower than female uptake for FOBT test (FIT) (OR 0.84; 95% confidence interval (CI), 0.75–0.95; p<0.05).[51] Although the acceptance of screening is low among male, the introduction of FIT instead of guaiac-based FOBT testing (gFOBT) has significantly increase CRC screening uptake with absolute differences of 8.1% (gFOBT 56.4% *vs* FIT 64.5%, OR 1.41, 95% CI 1.36-1.45) compared to women with absolute differences of 6.0% (gFOBT 62.1% *vs* FIT 68.1%, OR 1.31, 95% CI 1.27 to 1.34).[49]

A consistent ethnicity inequality in CRC screening uptake has been reported in previous literature. A population-based survey among respondents living in England reported that non-White participants were less likely to respond to screening invitation compared to White (41.5% *vs* 70.5%, p<0.001).[47] A cohort study following a screening outreach program from 2004 until 2013 found that the screening rate among minorities such as Hispanics (33.1 to 78.3%) and Native Americans (29.4 to 74.5%) remains low compared to White in both before and after the programme (35.2 to 81.1%).[52] Poor participation of minority ethnicity could be explained by low perceived susceptibility to CRC in non-English speaker especially among Asian and Hispanics.[4] Moreover, the low CRC screening uptake has resulted in an increased risk of late presentation of CRC among Black people (aOR 1.80, 95% CI 1.02-3.17, p<0.05) and Asian (aOR 1.41, 95% CI 0.97-2.05, p=0.07).[53]

Marital status was consistently associated with healthier behaviour and increased adherence to cancer screening. This is proved in a large population study conducted in the United Kingdom that found single people had lower CRC screening uptake compared to those who were married (55.7% *vs* 71.7%, p<0.001).[47] The findings are supported by the 2010 Behavioural Risk Factor Surveillance System Survey (BRFSS) analysis among adults in the United States whereby individuals who were divorced, separated, never married or widowed have lower odds to adhere to the CRC screening guidelines compared to married couples.[54] Another analysis of the BRFSS survey found that marital status is an independent predictor of cancer screening including CRC (OR 1.63, 95% CI: 1.51-1.77).[55] The findings are consistent with another study among Korean American in which married individuals are more likely to have sigmoidoscopy compared to unmarried (aOR 4.90, 95% CI: 1.09, 21.9, p<0.001). One of the mechanisms that explained the association of marital status with health behaviour is social control, which refers to regulatory attempts by others and feeling of responsibility or obligation towards others that facilitate the healthy behaviour.[56]

Education level

Education attainment has consistently associated with CRC screening uptake. Individuals with lower education level have lower screening participation compared to individuals with higher education level (65.7% *vs* 74.5%, p<0.001).[57] A contrary was reported in another study that stated education level is not associated with adherence to CRC screening after adjusted to other individuals covariates.[58] This is further supported by another study conducted in Korea that showed education level is not significantly associated with compliance to CRC screening recommendation.[59] A similar finding was also obtained from a population-based study in Hong Kong.[12] This is, however, contrary to a population-based study in the United States that found education level at grade 12, college 1-3 years, and college 4 years and above are more likely to participate in CRC screening (adjusted OR 1.4, 1.7 and 1.9 respectively with p<0.001) compared to those with lower education level.[5] A study in two Danish counties among average risk group for CRC screening found that higher education level was more likely to underwent FOBT screening (adjusted OR 1.38 (CI 95% 1.33-1.43, p<0.0001).[60]

Household income

There are several studies addressing the association between household income and CRC screening participation. A nationwide cross-sectional survey in Korea found that lower household income is significantly related to non-compliance to CRC screening (p<0.001).[59] The findings are consistent with a study in the United States that reported high household income is one of the significant predictors of current CRC screening (OR 1.9, p<0.001).[5] A large population study in Denmark also reported that individuals at first income quartile (annual household income of less than US Dollars 28,860.50) has higher odds of non-participation in screening recommendation using FOBT compared to individuals with fourth income quartile (OR 2.8, CI 95% 2.71-2.90).[61] The data are further supported by a study in 2 Danish counties whereby participation in FOBT screening is higher in high-income level (OR 1.94, CI 95% 1.87-2.01).[60]

Employment status

Several studies have established the relationship between employment status with the acceptance of CRC screening recommendation. Participants who were not in the labour force had more than two times higher odds to receive CRC screening (aOR 2.32, CI 95% 1.37-3.94).[3] This is similar to a study that showed people who are retired or out of work are more likely to have current CRC screening compared to people who are employed (adjusted OR 1.2, p<0.001).[5] Not in the labour force is defined as people who are currently unemployed and not seeking employment. Compared to people who are not in the labour force, employed individuals may be hindered from seeking health care including screening for cancer due to lack of sick leaves, the burden of taking days off work, and fear of negative consequences due to job insecurity.[62]

Interval visits to doctor for routine check-up

Several studies have been conducted examining the relationship between routine doctor visits with the uptake of CRC screening. In a study in the United States, patients who visited a doctor for routine check-up were more likely to receive up to date CRC screening in both colonoscopy or sigmoidoscopy (aOR = 2.6, p<0.001) and FOBT test (aOR = 6.2, p<0.001) compared to those who have not reported any routine check-up to a doctor for more than a year.[5] The findings are supported by a study among Korean American people at the age of 65 years old and older. This population have a more routine check-up of FOBT compared to those who did not have routine check-up (aOR 2.61, 95% CI 1.16, 5.9).[63] Individuals who did not have a routine check-up with a doctor are unlikely to undergo cancer screening as they are lacking in the opportunity to be screened, advised by doctors, and the opportunity to screening tools distributed in the clinic.

Comorbidities

Study regarding comorbidities and CRC uptake has been cited in several studies. A population-based study in Barcelona founds that individuals with three and more dominant chronic diseases were associated with low participation in the FOBT test (IRR 0.76, 95% CI 0.65, 0.89, p<0.001).[50] In another study among eligible screening adults found that individuals with type II diabetes were less likely to undergo screening using the FOBT test (aOR 0.703, 95% CI 0.557-0.887, p<0.001).[64] These show the role of multiple comorbidities as a barrier of CRC screening due to competing interest of healthcare provider to treat critical issue than recommending CRC screening.

Distance from clinic to house

The distance from the house to the nearest health facilities and its association with health has been cited in a few studies.[6,65,66] A study to identify the predictors of screening for cognitive impairment founds that the distance from the respondent's residential area is one of the significant predictors of screening participation. The distance of 2-2.99 km (aOR 0.62, 95% CI: 0.67-0.88) and 3km and more (aOR 0.54, 0.33-0.89) were less likely to participate in screening after adjusting the psychological and demographic factors.[6] A systematic review stated that out of 108 studies, 77% of studies have identified the distance decay association. This shows a negative correlation between travel distances to the nearest health facility with health outcome. Patients living far from healthcare facilities have been associated with negative health outcome such as low survival rate and longer hospital stay.[66]

Barriers of CRC screening participation

Several barriers have been identified that prevents people from getting screened for CRC including patient's factor, physician factor, and system factors. In a multicentre international study in Asia Pacific Region, a country with a low participation rate of CRC screening had low knowledge of CRC symptoms, risk factors, test, and lack of physician recommendation.[45] This is consistent in an FOBT specific test study conducted in Singapore. Most of the respondents (48.9%) identified not having CRC symptoms followed by inconvenience (31.1%), no family history of colon cancer (28.9%), lack of time (28.9%), and lack of reminders or recommendation (28.9%) are the reasons for not using FOBT [67]. Another study in the United States reported that 74% of the respon-

dents identified fear and bowel preparation are the most important barriers to colorectal screening. Patient's co-morbidity, previous refusal by patients, acute care clinic visits, lack of time, and lack of reminders has been identified as the most common physician reported barrier towards CRC screening.[68] Another study concluded that the most common barrier for CRC screening was lack of physician recommendation and lack of knowledge for the need of the test.[69]

Knowledge of CRC and screening

Knowledge is known to be important to influence the health-seeking behaviour and individual's preference to be screened for health condition including CRC. A study in West Malaysia found that less than 1% of respondents had undergo screening and most of their respondents have low knowledge score towards CRC and screening (only 4.1% of respondents have good knowledge score).[70] A multicentre study among Asia Pacific countries found that countries with low participation rate for CRC screening had the least knowledge on symptoms, risk factors, test, and the lowest recommendation by a physician.[45] The findings are consistent with another study that concluded respondents who are within the screening guideline is associated with better knowledge regarding CRC (p=0.001).[71]

Attitude towards CRC screening

Attitude is defined as a psychological tendency to view a subject with a degree of favour or disfavour. It is a process of individual subjective evaluation influenced by rational assessment, emotional responses, and belief.[72] Several studies have shown that attitudes may play an important role in cancer screening practices. A study in Geneva, Switzerland to explore the factors contributing to practice and attitude towards cancer screening found that the strong predictors of cancer practice are attitudes towards screening and towards prevention in general.[73] Another study that explores the reasons Netherlands have high CRC screening participation (prevalence of screening among the Netherlands are relatively high at 75%) were due to trust in the government, perception of the seriousness of cancer, preventive health screening, and the importance of one's health as the important factors of the public's view on CRC screening.[11] A study conducted in West Malaysia founds that majority of the participants have a poor attitude towards CRC screening and less than 1% of participants reported had undergone CRC screening.[70]

Conclusions

CRC incidence and mortality varied widely between countries. Generally, countries with high incidence and mortality of CRC experiencing inadequate uptake of CRC screening. There are various predictors that contribute to the inadequate screening uptake namely demographic inequality (age, gender, ethnicity, marital status), socioeconomic factor (education attainment, employment status, household income), frequency of visit to the healthcare provider, distance from health services, comorbidity, individual's knowledge and attitude toward CRC and its screening. Identification of these predictors and barriers for CRC screening is vital to develop an effective strategy to improve the screening uptake and ultimately for better health outcome of the population.

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