Screening Colonoscopy for Colon Cancer in Women during COVID-19 Pandemic

Muhammad Begawan Bestari, Ignatius R. Joewono

Division of Gastroenterology – Hepatology, Department of Internal Medicine, Faculty of Medicine Universitas Padjadjaran - Hasan Sadikin Hospital, Bandung, Indonesia.

Corresponding Author:
Muhammad Begawan Bestari, MD, MHS, PhD, FASGE, FACG. Division of Gastroenterology - Hepatology, Department of Internal Medicine, Faculty of Medicine Universitas Padjadjaran - Hasan Sadikin Hospital. Jl. Pasteur no.38. Bandung 40161, Indonesia. email: begawanb@yahoo.com.

ABSTRAK

Keganasan kolorektal merupakan salah satu dari tiga keganasan penyebab kematian tertinggi di dunia, namun dapat dideteksi secara dini dan dicegah melalui skrining. Beberapa pedoman merekomendasikan skrining dengan metode berbasis feses dan visualisasi langsung dengan kolonoskopi. Secara anatomis wanita memiliki kolon yang lebih panjang, terutama pada bagian kolon transversum, sehingga sulit dilakukan endoskopi menyeluruh. Pada wanita juga lebih banyak ditemukan keganasan pada kolon sisi kanan dengan jenis yang datar dan menjorok ke dalam sehingga lebih sulit dideteksi. Prosedur kolonoskopi seringkali dirasa tidak nyaman oleh wanita, terutama jika operator berjenis kelamin pria, sedangkan jumlah gastroenterologis wanita masih belum mencukupi. Pada masa pandemi COVID-19, pasien semakin enggan untuk melakukan skrining karena takut tertular. Keterlambatan diagnosis menyebabkan keganasan terdeteksi pada stadium lebih lanjut, sehingga menurunkan tingkat kelangsungan hidup. Ditambah lagi, ketika terdeteksi pada stadium lanjut, wanita memiliki tingkat kelangsungan hidup 1 tahun yang lebih rendah dibanding pria. Saat ini, telah banyak pilihan skrining lain yang baru dikembangkan seperti colon capsule endoscopy yang dapat dilakukan di klinik dan mengurangi kebutuhan untuk kolonoskopi, namun belum ada panduan klinis untuk skrining pada wanita. Tujuan dari tulisan ini adalah mengidentifikasi tantangan dalam melakukan kolonoskopi skrining pada wanita, terutama di masa pandemi, dan mendorong pengembangan panduan skrining untuk wanita.

Kata kunci: *keganasan kolorektal, kolonoskopi skrining, wanita, COVID-19.*

ABSTRACT

Colorectal cancer (CRC) is one of the top three leading causes of death in both men and women. However, screening can help detect and prevent CRC. Multiple guidelines recommend CRC screening using stool-based screening and direct visualization via colonoscopy. Anatomically, women have a longer total colonic length, especially in the transverse colon, which makes it redundant; thus it is more difficult to perform complete endoscopy in women. Women also have a higher risk of developing right-sided colon cancer of the flat and depressed type, which is harder to detect than the other types. Moreover, women are less likely to undergo colonoscopy due to embarrassment, especially when the procedure is performed by male gastroenterologists, and the lack of available female gastroenterologists further complicates the problem. The current COVID-19 pandemic also decreases patients' willingness to undergo screening due to the fear of contracting the COVID-19. Delay in diagnosis leads to more advanced tumors upon detection and ultimately decreases the survival rate, especially in women, as they have lower 1-year survival rate when CRC is detected in its later stages than in men. Innovative options for CRC screening have recently emerged, including colon capsule endoscopy, which can be performed in a clinic and may

reduce the need for colonoscopy. However, sex-specific CRC screening guidelines and tools are not available. The objective of this review is to identify the barriers and challenges faced when performing screening colonoscopy in women, especially during the pandemic and to encourage the development of sex-specific CRC screening.

Keywords: *colorectal cancer, screening colonoscopy, women, COVID-19.*

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide, accounting for 11% of all the cancers. In terms of mortality, CRC is the third leading cause of cancer-related deaths.[1] In the United States, although the incidence and mortality rates declined between 2007 and 2016 (by 2.4% and 2.2% each year, respectively), CRC still ranks as the third leading cause of cancer-related mortality,[2,3] and the incidence of colon cancer in younger populations is increasing.[4]

Multiple guidelines globally recommend that average-risk adults should undergo CRC screening starting at the age of 50-75 years, while some recommend that screening should start at the age of 45 years.[5,6] Available screening modalities currently comprise stool-based screening tests, including the fecal occult blood test (FOBT), guaiac-based FOBT, and fecal immunochemical test (FIT), and direct visualization methods, such as flexible sigmoidoscopy and colonoscopy. Among the available CRC screening methods, colonoscopy is the preferred modality because it provides high sensitivity for cancers and all classes of precancerous lesions, can deliver diagnostics and therapeutics in a single session, and has wide procedure intervals (10 years) for normal results[7,8] One or two normal colonoscopy results may imply lifetime protection from CRC.[9]

Colonoscopy is an invasive and uncomfortable procedure, especially for women. Previous reports have stated that patients' sex affects various aspects of CRC screening, from their attitude towards colonoscopy to anatomical and tumor behavior.[10-14] This paper will review the difficulties encountered when performing colonoscopy in women, the challenges faced by women, the current obstacles created by the COVID-19 pandemic, and possible future improvements for conducting CRC screening.

DIFFICULTIES PERFORMING COLONOSCOPY IN WOMEN

Anatomical Differences

One indicator for complete colonoscopy is the cecal intubation rate (CIR). As recommended by the US Multi-Society Task Force on Colorectal Cancer, the CIR should be above 95% for screening endoscopy and 90% for all examinations.[8] Previous studies have shown that female sex is a risk factor for incomplete endoscopy or a lower CIR rate.[15-18] Koido et al[17] stated that female sex is a significant risk factor for incomplete colonoscopy (Odds ratio (OR) = 1.38, 95% confidence interval CI: 1.17-1.64, P = 0.0002). Another study conducted with endoscopist trainees suggested that, in case of female patients, trainees are 1.5 times more likely to fail to intubate the cecum.[18] The difficulties encountered when performing complete colonoscopies in women has been described since the 1990s. These difficulties are caused by the longer colonic length in women than in men (155 cm vs. 145 cm), especially the length of the transverse colon (48 cm vs. 40 cm), which is also responsible for the redundancy of the segment causing sagging into the true pelvis more in women than in men (62% vs. 26%).[10,13,19]

Tumor Behavior in Women

The most common tumor location also differs according to patients' sex: in females, tumors are mostly located at the proximal/right-sided-colon while in males they tend to be located at the distal/left-sided-colon (55% and 44% respectively).[14] Hormonal factors may account for the frequent right-sided colon cancer (RCC) in women. The Women's Health Initiative Clinical Trial reported that post-menopausal women who received hormone replacement therapy (HRT) showed a 40% reduction in CRC risk; however, CRC

diagnosed in women receiving HRT was reported to be higher in grade and stage.[20] RCC has been reported to be more advanced in stage upon diagnosis and to have more poorly differentiated tumors.[21] A meta-analysis reported that left-sided colon cancer (LCC) was significantly associated with a reduced risk of death (Hazard ratio (HR), 0.82; 95% CI, 0.79-0.84; P<0.001), independent of stage, race, adjuvant chemotherapy, year the study was conducted, number of participants, and quality of study.[22] As women tend to have lower CIRs, it is possible that RCC can remain undetected during screening, and therefore present with an advanced stage when finally diagnosed. Moreover, a larger proportion of women develop flat and depressed type colorectal neoplasia, which can remain undetected and lead to late diagnosis, in contrast to men, who more commonly develop polypoid type of neoplasia that is easily detected and resected.[23]

CHALLENGES FOR WOMEN UNDERGOING CRC SCREENING

Women's Attitudes Toward Screening

The rates of participation in CRC screening differ by sex and are significantly lower in women. Previous studies have shown that CRC screening compliance is 7-9% lower in women than in men.[24] A report by Brawarsky et al,[25] indicated that men and women have an equal probability of receiving recommendations to undergo screening, but men were significantly more likely to complete the screening, suggesting that the barrier to screening was at the patient level. One main reason for this finding may be that women are embarrassed to undergo colonoscopy, especially when the procedure is performed by a male physician.[25] In Israel, women significantly tended to request for specific sex preference of the endoscopist than men (37% and 27%, respectively), and when sex preference was mentioned, the same sex was almost always preferred, with the most frequently stated reason being that patients had higher trusts in an endoscopist of the same sex.[26] Menees et al[27], reported that 43% of the female patients preferred female endoscopists, and of those, 87% were willing to wait for >30 days for the female endoscopists to become available. Furthermore, 14% of the female patients were willing to pay more fees, with embarrassment given as the main reason. This pattern of preference is consistent or even more prominent nowadays. The preference rate of same-sex endoscopists in Korea was 14.6% in 2008 in contrast to 24.9% in 2016, while the female patient preference for same-sex endoscopist increased by 95% (OR, 2.678; 95 CI, 1.418–5.057; P=0.002).[28] Furthermore, the gender of the endoscopy nurse assistant was also stated as a reason for women to delay screening endoscopy; for this reason the rate of women declining endoscopy was higher [74.5%; female (73.4%) and male (1.1%)] than men [overall 58%, male (49.3%) and female (8.7%); P < 0.001], with a third of patients stated that they would decline screening endoscopy if their request was not met.[29]

Female Gastroenterologists

Another factor that may worsen the barrier for women to undergo CRC screening is that the current number of available female gastroenterologists/endoscopists is much lesser than that of males, despite women's preference for female gastroenterologists. A report by the Association of American Medical Colleges (AAMC) regarding active physicians by sex and specialty in 2017 stated that, in the field of gastroenterology, 82.4% were male (n = 12,135) and 17.6% were female (n = 2,593).[30] The male gastroenterologists also worked for more hours per week than their female counterparts. A survey conducted with Canadian gastroenterologists found that male gastroenterologists on an average worked 6 hours/week more than female gastroenterologists did (58.3 SD 15.4 vs. 52.3 SD 11.8 hours/week, P = 0.025).[31] These findings are consistent with another survey by Singh et al, which reported that men worked 8 /week more than women did (54 vs. 46 hours/ week, P = 0.03) especially in non-academic practice.[31,32] However, the 2019 data have shown that the male-to-female ratio of internal medicine residents in the US does not differ greatly (57.7% male and 42.3% female). Therefore, it seems

that fewer females are willing to pursue further education in the field of gastroenterology as there were only 34.7% female gastroenterology fellows in the same year.[33] Nevertheless, this data suggests an improvement from previous reports, which stated that only 25-30% of the gastroenterology fellows were female.[34]

IMPACT OF THE COVID-19 PANDEMIC

We are currently living in difficult times due to the global pandemic of COVID-19, where the entire world, especially the medical field has been severely affected. The endoscopy team is at risk of contracting COVID-19 via inhalation, conjunctival contact and the fecal-oral route.[35,36] Since the pandemic started, professional societies have released guidelines regarding endoscopy, including a list of endoscopy procedures that should be postponed. Regarding screening colonoscopy, multiple gastroenterology professional societies recommend to postponement of all elective and non-urgent endoscopies.[37-39] Levin et al.[40] reported that organized CRC screening in California decreased the annual CRC incidence by 25.5% from 95.8 to 71.4 cases/100,000 ($P < 0.01$) between 2000 and 2015, and a 52.4% reduction in cancer mortality, from 30.9 to 14.7 deaths/100,000 ($P < 0.01$). Moreover, the CRC screening rate has substantially reduced due to the pandemic (by approximately 86%),[41] and, as the duration of the pandemic is unknown, new cancer cases will remain undiagnosed each day. Even after the pandemic is over, patients may still be reluctant to visit the hospital in order to undergo screening. This diagnostic delay will lead to cancer progression and risk of potential long-term effects including lower survival rates. Additionally, female patients will be more affected by the delay in diagnosis because, as reported by the UK cancer research, the 1-year survival rate after diagnosis of stage IV and III bowel cancer is 5% and 2% lower in females, respectively, than in males; but the 5-year survival rate does not significantly differ between the sexes at any stage.[42]

DISCUSSION

There are currently no sex-specific guidelines or tools for CRC screening, despite the differences in anatomy of the colon between the sexes. In women, the longer average total colon length and transverse colon length, as well as the more frequent occurrence of proximal tumors of the flat and depressed types may result in technical difficulties when performing endoscopic examinations. Therefore, it is necessary to emphasize the need to develop sex-specific CRC screening and customized tools for women.

Women's attitude towards undergoing screening colonoscopy should also be addressed, as the procedure is often considered embarrassing,

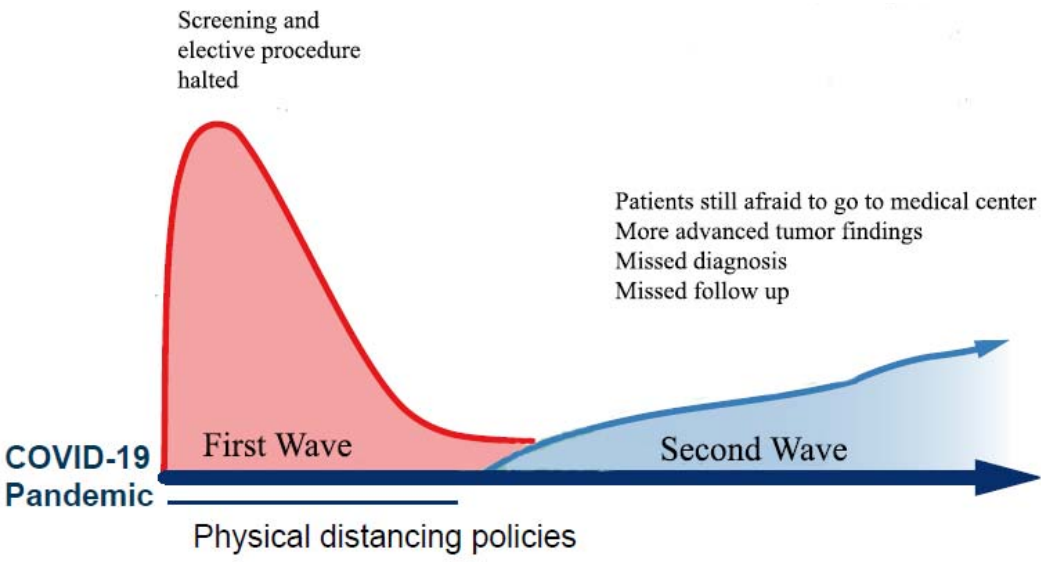

Figure. 1. The impact of COVID-19 pandemic on CRC screening. Adapted from Tapper and Asrani.[43]

inappropriate, and/or inconvenient. Education regarding the benefits of CRC screening should be integrated to reduce the negative stigma about colonoscopy. Patient assurance, especially for females, by the gastroenterologist (in particular male gastroenterologist) should be emphasized to increase patient compliance to undergo the procedure. Other strategies, such as having female nurse assistants may also be implemented. Furthermore, women's participation in the field of gastroenterology should be encouraged as the demand for female practitioners is high.

During this pandemic, the impact of not screening patients may have long-lasting consequences. Tapper and colleague, described the long-lasting impacts in cirrhosis care due to deferred screening in three waves.[43] A similar wave pattern may also be applied to CRC screening, and we predicted a two-wave model in this case (**Figure 1**). The first wave reflects the period in which all screening and elective procedures were halted. The second wave indicates the undiagnosed cases during lockdown and patients' reluctance to visit medical centers due to fear of contracting COVID-19 even after the pandemic has ended. The long-term consequence of this issue is a protracted period of suboptimal outcomes, including detection of more advanced tumors, missed diagnoses, and missed follow-up. Missed CRC screening can result in worse outcomes in women because as the tumor stage advances, the survival rate in women would drops even more compared that in men.[42]

On April 28, 2020, the American Society for Gastrointestinal Endoscopy (ASGE), released guidelines for resuming gastrointestinal endoscopy as the world approached the "post-lockdown" period.[44] The latest strategies are continually being developed to ease the workload when medical services return to normal, including an emphasis on noninvasive testing (e.g., FIT, gFOBT) and follow-up colonoscopy, with moderate priority being scheduled when the test results are positive.[45] Another option is to use the colon capsule endoscopy (CCE), which is indicated for patients with positive noninvasive screening. As CCE can be conducted by a healthcare provider in a clinic room, used for community screening, thereby reducing hospital attendance and possibly increasing patient compliance. In a recent study, CCE reduced colonoscopic surveillance by 43% when used as a primary test.[46] Thus the global pandemic may pave the way for CCE to be often used for screening and allow collection of more data regarding its effectiveness, safety, and cost. This newer strategy may elucidate CRC screening or change how CRC screening is performed in the future as it reduces the need for colonoscopy, thus providing women with more options. However, CCE only provides diagnostic information, so any positive result should ultimately be followed up by colonoscopy, thereby increasing the number of procedures and cost. A summary of the challenges faced by medical practitioners and female patients exacerbated by the current COVID-19 pandemic regarding screening colonoscopy is shown in **Figure 2**.

CONCLUSION

Multiple studies have shown the sex-related differences in colon cancer incidence and the colon anatomy; therefore, there is a need to develop sex-specific endoscopy. Furthermore, current CRC guidelines need to address the sex-specific problems in screening. Moreover, it is necessary to increase the number of practicing female gastroenterologists. To increase the number of female gastroenterologists, female internal medicine residents and medical students should be more encouraged to pursue career in gastroenterology. The difficulties for women are currently exacerbated by the pandemic situation, and medical providers should be more focused on finding a better and novel way to create more options, so that the gains of the past CRC screening are retained and the future of CRC screening, especially for women, may see a new light at the end of these dark times.

AUTHOR CONTRIBUTION

All authors M.B.B. and I.R.J. contributed equally in the conception and design, administrative support, provision of study materials or patients, collection and assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript.

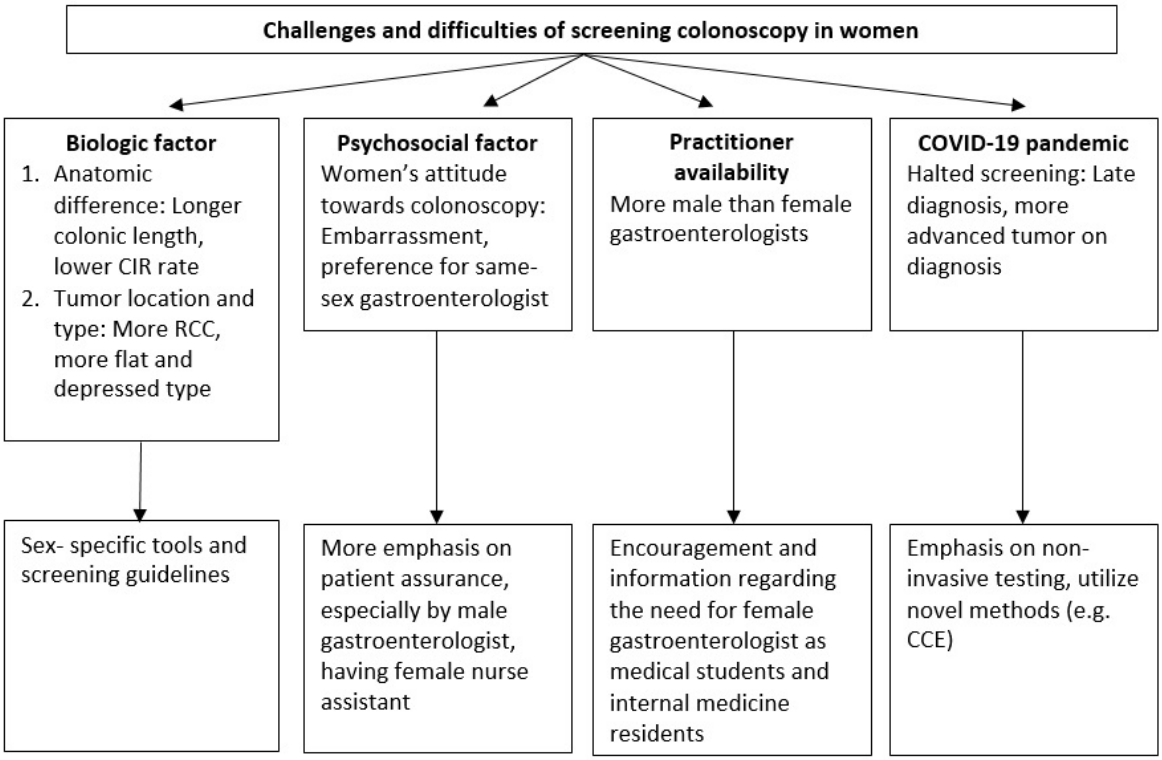

Figure 2. Summary of challenges and difficulties in screening colonoscopy in women. CIR: cecal intubation rate; RCC: right-sided colon cancer; CCE: colon capsule endoscopy.

ACKNOWLEDGMENTS

The authors would like to thank Editage for English language editing. The writing of this manuscript was carried out without funding.

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