Original Article

A 5-year evaluation of early-and late-onset sporadic colorectal cancer screening in Central Saudi Arabia

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Abstract

Background: The Al-Kharj colorectal cancer (CRC) screening program was implemented for five years (2017-2022) in a central urban area of Riyadh Province, Saudi Arabia, to assess the participation and impact of the program in average-risk individuals.

Methods: The high sensitivity-guaiac based-fecal occult blood test (HSgFOBT) was used as a first-line investigation to identify asymptomatic patients, aged 45–75 years, requiring CRC screening using colonoscopy. The program was run in three tertiary hospitals in the area.

Results: The five-year participation rate was 73% (35,640/48,897). The average age was 53 years (range 45–75), 49% were female (17,464/35,640), all were asymptomatic, and 77% had adequate bowel preparation. The HSgFOBT (+) rate was 6.3% (n = 2245), and 76% (n = 1701) of these underwent colonoscopy. The prevalence of findings were as follows: CRC, 4.8% (81/1701); advanced adenoma, 9.5% (162/1701); adenoma, 15.9% (270/1701); non-adenomatous polyps, 7.9% (135/1701); and no polyps or tumors, 25.4% (432/1701). Among participants aged 45–50 years, early onset-CRC had female predominance, while those ≥50 years with late onset-CRC were predominantly male. CRC was more prevalent in the left colon ($P < 0.005$).

Conclusions: Approximately one-third of the participants diagnosed with CRC had early-onset CRC. Screening participation was desirable for the defined target population. Public education is necessary along with expanded colonoscopy resources to continue further citizen participation.

Keywords: Advanced adenomas, colonoscopy, colorectal cancer screening, early onset

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide. In the U.S. and most Western European countries, CRC is the second leading cause of cancer-related death.[1,2]. In Saudi Arabia (SA), it is the second most commonly reported malignancy,[3,4] ranking first among men (10.6%) and third among women (8.9%).[5] The incidence of CRC has increased recently among young people (aged <50 years).[6,7] The underlying reasons are unknown but include genetic abnormalities such as germline mutations, which is referred to as early-onset CRC (EO-CRC).[8] One in five young patients with EO-CRC carries a mutation associated with cancer predisposition.[9] Population-based registries from high-income countries such as Australia, Canada, Denmark, Norway, New Zealand, Ireland, and the United Kingdom show that the incidence of CRC is decreasing in the more than 50-year-old individuals and but increasing in the younger age groups.[10] Late onset-CRC (LO-CRC), as reported in a retrospective study from 2001 to 2016 using the Saudi National Registry, and in the Northern region of the country, showed a similar trend of decreasing and increasing late- and early-onset CRC, respectively, in SA.[6,7]

The Saudi Cancer Registry (http://www.scr.org.sa/) indicated a rise in CRC frequency from 2001 to 2006, this rate was twice the incidence observed from 1994 to 2001[11]; however, no data was available assessing the trend in EO-CRC. At diagnosis, young Saudis presented with advanced-stage CRC and poor outcomes[3,7,12]; however, SA has no nationwide strategy for CRC screening despite the well-established increasing incidence in Saudis under 50 years of age, which reflects 85% of the population.[7,13,14]

The global interest lies in whether CRC becomes the most common cause of EO-CRC death.[15] Clinical practice guidelines for CRC screening have been published in SA since 2015.[16] The authors targeted asymptomatic people with an average risk for CRC in the general Saudi population starting at the age of 45 years, to be performed up to the age of 70 years. Colonoscopy is the "gold standard" for CRC screening and is recommended every 10 years. An alternative to colonoscopy—sigmoidoscopy screening—is recommended every 5 years. Endoscopy-based practices can be combined with a fecal immunochemical test (FIT) annually or every 3 years without an annual FIT.

In Europe, although practice varies by country, screenings with FIT and the guaiac based fecal occult blood test (g-FOBT) are considered every 1–2 years, and screening programs use both the g-FOBT and sigmoidoscopy or colonoscopy. Screening should start for everyone at the age of 50 and be performed in 1 to 2-year intervals up to 75 years of age.[17-19]

Recently, updated guidelines published in the U.S. have included CRC screening for young people.[15,16,20,21] The American guidelines[15] suggest that adults aged >45–75 years with an average risk for CRC should undergo non-invasive screening using either a high sensitivity stool based test or an invasive diagnostic method such as structural (visual) examination (e.g. colonoscopy or sigmoidoscopy), and for those aged 76-85 years procedures should be performed based on the individual's preference. Individuals with positive non-invasive screening test results should undergo a timely colonoscopy. Barriers to timely colonoscopy completion following an abnormal FIT or g-FOBT can occur at different transitions in care such as abnormal g-FOBT or FIT-result communication, scheduling/completion of colonoscopy, and receipt of results; all these vary by patient characteristics. The options for CRC screening are; a) non-invasive tests (FIT annually, g-FOBT annually, and multi-genes panel stool DNA test every 3 years); and b) invasive tests (computed tomography colonography every 5 years, flexible sigmoidoscopy every 5 years, and colonoscopy every 10 years). In this study, the Al-Kharj CRC-screening program analyzed the outcome of 5 years of screening for individuals with an average risk for CRC in a central region of SA, the Riyadh Province Al-Kharj, an urban city of 425,300 inhabitants.

PATIENTS AND METHODS

Study design

The study was conducted according to the STROBE statement. The Ethics Committee of PSAU University of Medical Sciences approved the study design, protocols, and informed consent procedure (PSAU/COM/RC/IRB/p/67).

We adopted a CRC screening program in Riyadh Province Al-Kharj of SA, offering free screening to all individuals aged 45–75 years. This was a population-based prospective study of individuals with registered addresses in Al-Kharj, who were invited by their general practitioner or internist or via email or social media (Twitter) to participate in the colorectal cancer screening program (CRCSP). This program followed the updated AGA guidelines[15] for CRC screening and was performed from January 2017 to February 2022. The informed consent and invitation letter described the exclusion and inclusion criteria and included a two-page small instruction cartoon explaining the sample collection process. Participants were identified prospectively via

Public Health Registries and invited randomly, according to birth month. The 5-year outcomes of colonoscopy screening as of February 2022 were collected. Those with a positive stool-based high-sensitivity guaiac-based fecal occult blood test (HSgFOBT) underwent annual colonoscopies. Data on demographic details including age, sex, and addresses of the participants was collected.

Data on the CRCSP participants were collected from a database of endoscopy reports at the Endoscopy Unit of King Khaled Hospital and Prince Sultan Centre for Health Care, Prince Sattam bin Abdulaziz University Hospital, and Al Kharj Military Hospital.

Patients: inclusion and exclusion criteria

All individuals were invited to participate in the CRCSP of Al-Kharj from 2017 to 2022. Participants in this cohort were selected based on birth month, and thus this population sample represents the outcomes of the entire first screening round. Asymptomatic individuals aged 45–75 years willing to begin CRC screening at age 45 were enrolled.

Individuals were excluded if they were: 1) symptomatic, 2) had inaccessible health records, 3) moved out of Al-Kharj during the observation period, 4) were aged >75 years, 5) had blood in the stool at the time of the interview, 6) had a previous CRC diagnosis, colonic resection, or any CRC chemotherapy or radiotherapy, and 7) had other colon diseases including colitis, diverticulitis, inflammatory bowel disease, or an indication for polypectomy. Additionally, individuals with a history of hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP), were excluded from the first non-invasive assessment.

Screening methods

Non-invasive assessment

Stool analysis used the high sensitivity guaiac fecal occult blood test (HSgFOBT). Annual screening was recommended if the HSgFOBT test result was negative. Those undergoing the HSgFOBT were instructed to avoid certain medications and food for several days before collection of stool samples. The patients collected samples over three separate bowel movements. For each sample, the collected stool was stored in a clean container provided by the lab. Lab analysis was performed according to the manufacturer's instructions using the HSgFOBT kit (Epitope Diagnostics Inc, USA). Individuals with an HSgFOBT indicating >100 μg hemoglobin/L were advised to undergo colonoscopy.

Structural screening

Patients with positive g-FOBT results underwent the relevant scope-based evaluation. Endoscopic evaluation employed lower gastrointestinal (GI) endoscopy (video-endoscope, GIF-160; Olympus Co., Tokyo, Japan) by a single experienced endoscopist. If the colonoscopy could not be completed, then a repeat procedure under propofol sedation was scheduled.

Tissue sampling

Tissue was sampled only when necessary, to confirm abnormal mucosal findings from the endoscopy. The samples were fixed in 10% formalin and labelled with the participant's identifier. A blinded pathologist analyzed the tissue samples to decrease measurement bias., Five outcomes were possible based on histological diagnosis: 1) CRC, 2) advanced adenoma (high risk), (adenoma with significant villous features [>25%], size >1.0 cm or more, high grade dysplasia, or early invasive cancer) 3) non-advanced adenoma (benign or non-cancerous polyp, medium-low risk adenoma) 4) serrated polyps, hyperplastic polyps (non-adenomatous polyps) 5) normal mucosa (no polyps or tumors), and 6) other non-relative findings (e.g. hemorrhoids, diverticulitis, colitis). For those with advanced adenoma, we suggested surveillance after 1 year; for those with adenoma, after 3 years; for those with serrated polyps, every 1–2 years; and for those with hyperplastic polyps, every 10 years. All participants entered a surveillance program.

Statistical analysis

Continuous variables were presented as means (SD) and minimum and maximum values, and categorical variables were presented as number (n) and frequencies (%) mean, SD, and minimum and maximum values. Comparison between groups was performed using t-test and chi-square test. All analyses were performed using SPSS v24 (Chicago, IL, USA). The demographic information included age and sex. *P* values less than 0.05 were considered statistically

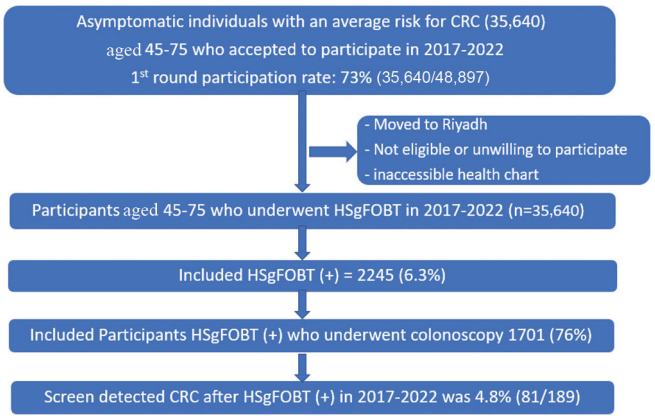

Figure 1: Flow chart of participants included in the study

Table 1: First-round processing times

Time until the g-FOBT result: 3.4 workdays
Time until intake: 11.2 workdays
Time until colonoscopy: 13.4 workdays
Six weeks between participation and colonoscopy

significant. Multiple linear regression was used to investigate the relationship between CRC prevalence and age groups, both in males and females.

RESULTS

The CRCSP was implemented in early 2017 through January 2022. During this period, 48,897 individuals were invited to participate, based on inclusion and exclusion criteria, in a CRC screening program established for outpatient clinics of family medicine and gastroenterology at three major tertiary hospitals in Al-Kharj: King Khaled Hospital and Prince Sultan Centre for Health Care, Prince Sattam bin Abdulaziz University Hospital, and the Al Kharj Military Hospital. The first-round participation rate was 72.8% (35,640/48,897). The participant enrolment is shown in Figure 1. The processing times for the first run are shown in [Table 1]. No complications were reported, and there were no cases of delayed colonoscopy despite the limitations of Covid-19 on cancer screening. But, there was a lower rate of participation in the pandemic period 2019-2020.

Of the 35,640 participants involved in the first round of the CRCSP, 2245 had positive HSgFOBT results in the first non-invasive assessment. This translates to a HSgFOBT positivity rate of 6.3% (2245 individuals positive). Of these, only 76% (1701) underwent a lower GI endoscopy. The rest declined due to the invasiveness of the procedure, personal and health factors, and travel. These patients were followed-up by their family doctor. No follow-up records were kept by the endoscopy units.

Of the 1,701 patients who underwent the secondary assessment (i.e. lower GI endoscopy), the average age was

Table 2: The results of linear regression tests between gender and CRC prevalence rate for every age group

Age groups	Regression Coefficient	*P*	R^2
45–50	<0.001	0.002	0.06
51–55	−0.003	0.003	0.07
56–60	−0.002	0.001	0.27
61–65	−0.34	0.001	0.37
66–70	−1.18	0.001	0.56
70–75	−2.03	0.001	0.62

58 years (range 45–75), with approximately 60% (1026/1701) of individuals aged <70 years, and 49% (837/1701) being women. All participants who underwent secondary assessment were asymptomatic (average risk for CRC); 13% (216/1701) underwent sigmoidoscopy due to intolerance of colonoscopy and eventually underwent a scheduled colonoscopy under propofol sedation; 77% (1323/1701) had adequate bowel preparation.

The prevalence of findings were as follows: CRC, 4.8% (81/1701); advanced adenoma, 9.5% (162/1701); adenoma, 15.9% (270/1701); non-adenomatous polyps, 7.9% (135/1701); and no relative findings, 25.4% (432/1701) [Figure 2]. Other non-relevant findings were internal hemorrhoids in 32% (540/1701), colitis in 24% (405/1701), diverticulosis in 7.9% (135/1701), and diverticulitis in 2.6% (27/1701). The sex distribution of endoscopic findings showed a significant male predominance ($P = 0.002$) [Figure 3]. The age distribution showed a significant predominance of CRC among individuals aged less than 50 years ($P = 0.0001$) [Figure 4]. Approximately 30% (24/81) of those aged 45–75 years showed early-onset CRC (45–50 years), with a female predominance (16/24, 66%) ($P = 0.001$). EO-CRC was significantly higher than late-onset cancer (>50 years) based on age group 51–55 years (13% [12/81]), 56–60 years (16% [13/81]), 61–65 years (11% [9/81]), 66–70 years (13%, [11/81]), and 71–75 years (15%, [12/81]), ($P = 0.0001$). This

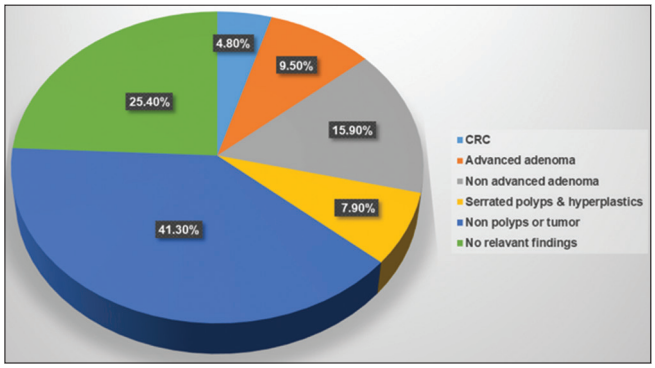

Figure 2: Frequency distribution of the endoscopy findings

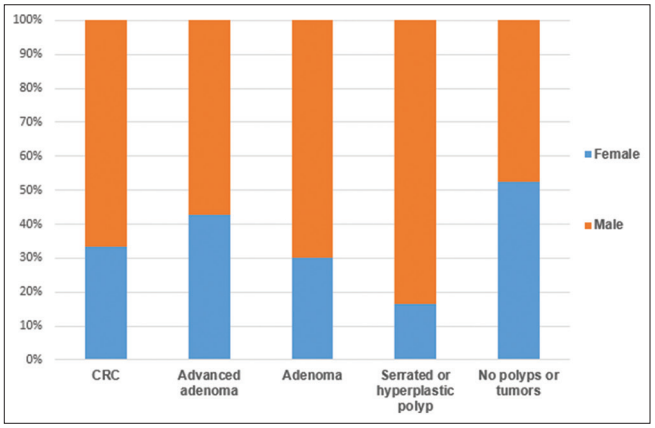

Figure 3: Sex distribution of the endoscopy findings

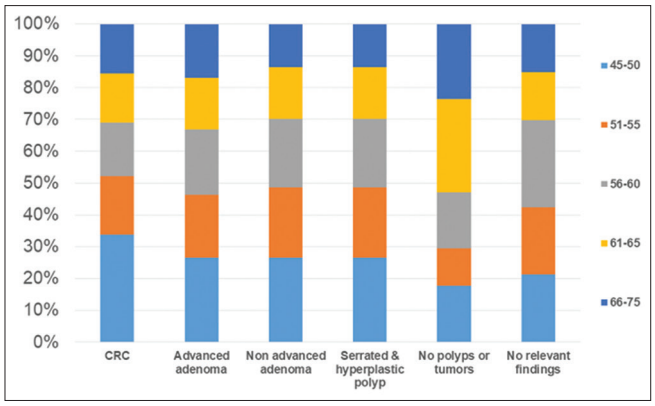

Figure 4: Age distribution of the endoscopy findings

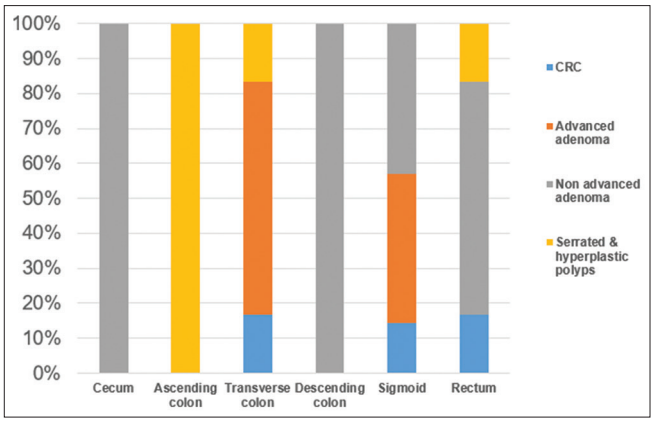

Figure 5: Site distribution of the endoscopy findings

comparison shows an increasing prevalence of EO-CRC versus LO-CRC by age groups. Regression models for each age group between gender and CRC prevalence showed a strong inverse association for older age groups compared to younger age groups (<50 years) [Table 2]. LO-CRC had a significant male predominance (59%, [36/61]), [P = 0.01]). The overall adenoma detection rate was 25.40% for our mixed gender study population indicating high quality in colonoscopy. CRC and polyps were significantly more frequently located in the left colon (P = 0.004) [Figure 5].

DISCUSSION

Differences in CRC screening strategies exist due to differences in geographic variation of CRC prevalence, available funds, and health infrastructure.[21,22] There are major health impacts, and economic effects of early detection are substantial.[23,24] However, many countries still lack effective national CRC prevention and screening programs. There has been a nationwide CRC screening program in SA,[25] and data from the national registry for EO-CRC and LO-CRC before 2017.[6] To the best of our knowledge, the first CRC screening program after 2017 was implemented in Al-Kharj Riyadh province, a central urban area of SA. The CRCSP was implemented for almost 5 years to help prevent CRC in the selected region and its surrounding areas in SA.

CRC screening programs using pure endoscopy and pathology are not appealing to a wide range of people because of its invasive nature.[26] This leads to reduced participation, and in our study, 20% of the individuals refused to undergo colonoscopy despite positive HSgFOBT results. A recent study[27] reported that approximately 33% of scheduled colonoscopies were postponed during a period of 16 months because of personal, social, geographic, and health system factors. Here, the performance of colonoscopy was within two weeks; there was no delayed colonoscopy after the initial positive HSgFOBT considering that such delay is associated with poor CRC outcomes.[28] Second-round CRC screening was continued according to recommendations.[15]

In a local study, 71% of Saudis preferred CRC screening using the following modalities in descending order: CT colonography (CTC), stool-based test, colonoscopy, and flexible sigmoidoscopy.[29] As in our study results, there was a preference for HSgFOBT and then scope-based methods.[29] Furthermore, based on their investigation of CRC awareness among healthy individuals in SA, Zubaidi *et al*.[4] (2015), strongly recommended implementing a countrywide policy including an education/screening program to improve CRC awareness. Reasons included misconceptions regarding universally accepted screening protocols, atypical symptoms, and general awareness on CRC. However, this approach has been challenged by a national survey that found that it is more complex than just knowledge-related issues, and that there may be other barriers that need to be addressed.[30]

There is a lack of national data after 2017 in SA on the frequency of adenomatous polyps and the age groups most affected. The prevalence of lesions in our study were 4.8% for CRC, 9.5% for advanced adenoma, 15.9% for adenoma, 7.9% for non-adenomatous polyps, and 25.4% for no relative findings. Similar findings were reported by a recent study using the Saudi National Registry between 2001 and 2016, thus showing an increase in early-onset cancer with female predominance and an increase in late-onset CRC.[6]

Another retrospective cohort study reported adenomas at 8.1% and advanced adenomas at 0.5%.[31] Most adenomas (33.9%) were located in the left colon. Similar results from a retrospective study showed that 25% of the patients were diagnosed with rectal tumors (42.89% located

in the left colon).[32] In our study, most adenomas (33.9%) were also located in the left colon. A higher prevalence rate of CRC was reported in older studies[6,32] versus the lower prevalence rates reported in our study. This might be because we included a general population being screened for CRC, in a different geographic region; our study was after the year 2017 and had a different age and sex distribution.

A recent retrospective study from 2009 to 2017 reported a significant increase in the incidence of late-onset CRC between 2009 and 2011 (28.46%), and between 2012 and 2014 (35.47%), followed by a drop of 32.51% between 2015 and 2017.[32] Another study reported a decrease in late-onset cancer at ages >50 years.[33] Compared with an older study in 2004,[31] the highest ASR was much higher in the Riyadh region 9.6/100,000. Other areas with high ASR were the Eastern region (9.8/100,000), Northern region (9.6/100,000), Makkah region (7.4/100,000), and Tabuk region (8.2/100,000). The median age at diagnosis was 60 years among men, with ages between 19 and 105 years, and 58 years among women, with ages between 16 and 100 years. The ASR has decreased in those aged >50 years; however, EO-CRC is much more prevalent than LO-CRC, as shown by Saudi studies[6,31] similar to our recent updated findings after 2017. CRC screening in Saudi Arabia, despite the low ASR, is cost effective, as noted in a recent cost-effective analysis.[34]

A meta-analysis of six observational studies (2008) reported evidence of low-quality colonoscopy including 34 serious complications per 100,000 CRC screening procedures.[35] Specifically, 2.8 serious complications per 1,000 were reported, including perforation, bleeding, and even death. The authors concluded that invasive CRC screening modalities should only be undertaken at specialized centers with skilled and experienced clinical staff for advanced therapeutic endoscopy. However, no complications were reported in our study.

The first round of non-invasive assessment using the g-FOBT highlighted the strengths and weaknesses of the current clinical practice: about 1/3 of the participants had no opportunity to participate due to the low number of referrals for CRC, the use of a non-invasive CRC screening test, and the unwillingness of HSgFOBT-positive individuals to proceed for invasive tests. However, there was a high screening participation, desirable for the defined target population in SA relative to the international guidelines.[15] A high number of patients at risk for CRC referred for endoscopy provided by local endoscopy services in the Al-Kharj area, Combined with the second structural screening for CRC it will help to decrease the incidence of CRC in Al-Kharj, through early detection of premalignant and early-stage cancers before they become advanced. The outcome of CRC strongly depends on the stage at which it is detected; thus, those at risk for CRC must be motivated to undergo endoscopy.

The limitation of this study is that it adopted the CRCSP in Al-Kharj, a rural area outside of Riyadh, which itself is a central urban rural area of SA. Though the area of sample collection and the sample size were small, there is no limitation in applying the program in more hospitals in Riyadh for better participation, over a longer period preceded by public awareness and education. Other limitations to consider include survivor cancer care and availability of molecular characterization of tumors as well as testing necessary to improve the outcomes of young patients with CRC. The assessment of patient-level information such as education, income, obesity, and physical activity was not performed because our analysis was based on aggregate data that was still useful for assessing cancer rate trends.

One of the strengths of our study is that no other prospective study has yet assessed the trends in CRC incidence among Saudis <50 years—representing 85% of the population. Our study showed low CRC prevalence rates from 2017 to 2021 compared to earlier years. However, no data from the areas surrounding Riyadh are available, and there are no data available after 2017 even for Riyadh, the populous capital of SA. The decrease in incidence could be attributed to the policy of population-based CRC screening since the initial CRC guidelines were published in 2015. Other studies have also shown a high incidence of early-onset CRC, with a female predominance. One retrospective study was from the northern area of SA, representing all available colorectal cancers during a period of 10 years,[7] and another one was from the Saudi National Registry before 2016.[6] Our study reflects the global concern for early-onset CRC[15] with poor outcomes.[36]

In conclusion, this 5-year outcome of CRCSP at a central rural region of SA, Al-Kharj, Riyadh Province, showed a low prevalence of CRC and advanced adenomas compared to that of previous studies in other geographic regions of SA, before 2017. Here, the implemented program highlights a fall in late-onset CRC incidence but a significant increase in early-onset CRC. Participation in CRC screening was high. Consequently, a public education program is highly recommended along with endoscopy resources to enhance and continue participation of citizens for CRC screening.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Howe HL, Wu X, Ries LA, Cokkinides V, Ahmed F, Jemal A, *et al.* Annual report to the nation on the status of cancer, 1975-2003, featuring cancer among U.S. Hispanic/Latino populations. Cancer 2006;107:1711-42.
2. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, *et al.* Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-30.
3. Mosli MH, Al-Ahwal MS. Colorectal cancer in the Kingdom of Saudi Arabia: Need for screening. Asian Pac J Cancer Prev 2012;13:3809-13.
4. Zubaidi AM, AlSubaie NM, AlHumaid AA, Shaik SA, AlKhayal KA, AlObeed OA. Public awareness of colorectal cancer in Saudi Arabia: A survey of 1070 participants in Riyadh. Saudi J Gastroenterol 2015;21:78-83.
5. Al-Ahwal MS, Shafik YH, Al-Ahwal HM. First national survival data for colorectal cancer among Saudis between 1994 and 2004: What's next? BMC Public Health 2013;13:73. doi: 10.1186/1471-2458-13-73.
6. Alyabsi M, Algarni M, Alshammari K. Trends in colorectal cancer incidence rates in Saudi Arabia (2001-2016) using Saudi National Registry: Early-versus late-onset disease. Front Oncol 2021;11:730689. doi: 10.3389/fonc. 2021.730689.
7. Alharbi SH, Alshammari KI, Alanazi KK, Ahmed HG. Patterns and grades of presentation of colon cancer in Northern Saudi Arabia. Prz Gastroenterol 2021;16:235-9.
8. Siegel RL, Jakubowski CD, Fedewa SA, Davis A, Azad NS. Colorectal cancer in the young: Epidemiology, prevention, management. Am Soc Clin Oncol Educ Book 2020;40:1-14. doi: 10.1200/EDBK_279901.
9. Stoffel EM, Koeppe E, Everett J, Ulintz P, Kiel M, Osborne J, *et al.* Germline genetic features of young individuals with colorectal cancer. Gastroenterology 2018;154:897-905.e1.
10. Araghi M, Soerjomataram I, Bardot A, Ferlay J, Cabasag CJ, Morrison DS, *et al.* Changes in colorectal cancer incidence in seven high-income countries: A population-based study. Lancet Gastroenterol Hepatol 2019;4:511-8.
11. Ibrahim EM, Zeeneldin AA, El-Khodary TR, Al-Gahmi AM, Bin Sadiq BM. Past, present and future of colorectal cancer in the Kingdom of Saudi Arabia. Saudi J Gastroenterol 2008;14:178-82.
12. Aljebreen AM. Clinico-pathological patterns of colorectal cancer in Saudi Arabia: Younger with an advanced stage presentation. Saudi J Gastroenterol 2007;13:84-7.
13. Sibiani AR, Shaheen M, Fallatah HI, Akbar HO, Qari YA, Bazaraa S, *et al.* Colorectal Cancer in Saudi Arabia King Abdul Aziz University Hospital: A Five Year Experience. J Med Med Sci 2011;2:1126-30.
14. Aljumah AA, Aljebreen AM. Policy of screening for colorectal cancer in Saudi Arabia: A prospective analysis. Saudi J Gastroenterol 2017;23:161-8.
15. Wolf AMD, Fontham ETH, Church TR, Flowers CR, Guerra CE, LaMonte SJ, *et al.* Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin 2018;68:250-81.
16. Alsanea N, Almadi MA, Abduljabbar AS, Alhomoud S, Alshaban TA, Alsuhaibani A, *et al.* National guidelines for colorectal cancer screening in Saudi Arabia with strength of recommendations and quality of evidence. Ann Saudi Med 2015;35:189-95.
17. Zavoral M, Suchanek S, Zavada F, Dusek L, Muzik J, Seifert B, *et al.* Colorectal cancer screening in Europe. World J Gastroenterol 2009;15:5907-15.
18. European Colorectal Cancer Screening Guidelines Working Group, von Karsa L, Patnick J, Segnan N, Atkin W, Halloran S, *et al.* European guidelines for quality assurance in colorectal cancer screening and diagnosis: Overview and introduction to the full supplement publication. Endoscopy 2013;45:51-9.
19. Recommendations on cancer screening in the European Union. Advisory Committee on Cancer Prevention. Eur J Cancer 2000;36:1473-8.
20. Patel SG, May FP, Anderson JC, Burke CA, Dominitz JA, Gross SA, *et al.* Updates on age to start and stop colorectal cancer screening: Recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc 2022;95:1-15. doi: 10.1016/j.gie. 2021.06.012.
21. Schreuders EH, Ruco A, Rabeneck L, Schoen RE, Sung JJ, Young GP, *et al.* Colorectal cancer screening: A global overview of existing programmes. Gut 2015;64:1637-49.
22. Carethers JM, Doubeni CA. Causes of socioeconomic disparities in colorectal cancer and intervention framework and strategies. Gastroenterology 2020;158:354-67.
23. Mendivil J, Appierto M, Aceituno S, Comas M, Rué M. Economic evaluations of screening strategies for the early detection of colorectal cancer in the average-risk population: A systematic literature review. PLoS One 2019;14:e0227251. doi: 10.1371/journal.pone. 0227251.
24. Smith HA, Scarffe AD, Brunet N, Champion C, Kandola K, Tessier A, *et al.* Impact of colorectal cancer screening participation in remote northern Canada: A retrospective cohort study. World J Gastroenterol 2020;26:7652-63.
25. Available from: https://www.moh.gov.sa/en/Ministry/Projects/Colorectal-Cancer-Awareness/Pages/default.aspx.
26. Smith H, Brunet N, Tessier A, Boushey R, Kuziemsky C. Barriers to colonoscopy in remote northern Canada: An analysis of cancellations. Int J Circumpolar Health 2020;79:1816678. doi: 10.1080/22423982.2020.1816678.
27. Flugelman AA, Stein N, Segol O, Lavi I, Keinan-Boker L. Delayed colonoscopy following a positive fecal test result and cancer mortality. JNCI Cancer Spectr 2019;3:pkz024. doi: 10.1093/jncics/pkz024.
28. Gupta S, Lieberman D, Anderson JC, Burke CA, Dominitz JA, Kaltenbach T, *et al.* Recommendations for follow-up after colonoscopy and polypectomy: A consensus update by the us multi-society task force on colorectal cancer. Gastroenterology 2020;158:1131-53.e5.
29. Almadi MA, Mosli MH, Bohlega MS, Al Essa MA, AlDohan MS, Alabdallatif TA, *et al.* Effect of public knowledge, attitudes, and behavior on willingness to undergo colorectal cancer screening using the health belief model. Saudi J Gastroenterol 2015;21:71-7.
30. Almadi MA, Alghamdi F. The gap between knowledge and undergoing colorectal cancer screening using the Health Belief Model: A national survey. Saudi J Gastroenterol 2019;25:27-39.
31. Almadi MA, Alharbi O, Azzam N, Wadera J, Sadaf N, Aljebreen AM. Prevalence and characteristics of colonic polyps and adenomas in 2654 colonoscopies in Saudi Arabia. Saudi J Gastroenterol 2014;20:154-61.
32. Alyabsi M, Sabatin F, Ramadan M, Jazieh AR. Colorectal cancer survival among Ministry of National Guard-Health Affairs (MNG-HA) population 2009-2017: Retrospective study. BMC Cancer 2021;21:954. doi: 10.1186/s12885-021-08705-8.
33. Cancer incidence report, 1999-2000 2004. National Cancer Registry. Kingdom of Saudi Arabia: Ministry of Health. Available from: https://nhic.gov.sa/eServices/Documents/Incidence%20Report%202004.pdf.
34. Naber SK, Almadi MA, Guyatt G, Xie F, Lansdorp-Vogelaar I. Cost-effectiveness analysis of colorectal cancer screening in a low incidence country: The case of Saudi Arabia. Saudi J Gastroenterol 2021;27:208-16.
35. U.S. Preventive Services Task Force. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2008;149:627-37.
36. Rahib L, Wehner MR, Matrisian LM, Nead KT. Estimated projection of US cancer incidence and death to 2040. JAMA Netw Open 2021;4:e214708.