International Journal of Community Medicine and Public Health
Saeed MF et al. Int J Community Med Public Health. 2022 Jun;9(6):2709-2717
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20221558

Review Article

Inherited bowel cancer: a review from a surgeon's perspective

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Received: 05 April 2022
Revised: 07 May 2022
Accepted: 09 May 2022

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ABSTRACT

Colorectal cancer (CRC) is the second most deadly cancer affecting globally. Although most CRCs seen in young adults are sporadic, hereditary cancer syndromes should be considered as an essential factor. Screening for colorectal cancer aids in the early detection and treatment of early-stage CRC; which reduces mortality rates. This review article aimed to present neoplastic and non-neoplastic polyps and their management from a surgeon's perspective while describing screening protocols in high-risk groups. It also highlighted the etiology, clinical features, diagnosis and management of adenomatous polyps and hereditary bowel cancer syndromes like Peutz-Jeghers syndrome (PJS), juvenile polyposis syndrome (JPS), Cowden syndrome (CS), Lynch syndrome (LS) and familial adenomatous polyposis (FAP). The article summarized the importance of these syndromes as a risk factor in colorectal cancer and identifies these as high-risk group patients in colorectal screening protocols. A summary of the management of these risk factors has been described from a surgeon's point of view.

Keywords: Neoplastic and non-neoplastic polyps, PJS, JPS, CS, LS, FAP

INTRODUCTION

CRC is considered the third most common neoplasm and the second most deadly cancer affecting both males and females globally, after lung and breast cancer.[1] In a study published by Siegel et al in 2017, it was found that CRC rates have been increasing annually in individuals aged 20-39 and 40-54 since the mid-1980s and mid-1990s, respectively, using surveillance, epidemiology, and end results (SEER) program data.[2] While a decline has been noted over the past few decades in the older population.

Most CRC cases diagnosed in young adults are sporadic. Still, some are due to hereditary cancer syndromes like: FAP, hereditary non-polyposis colon cancer (HNPCC), PJS and FAP.3 Modifiable risk factors such as obesity, lack of exercise, poor dietary habits and alcohol consumption have been attributed to the increasing prevalence of CRC.[4] In addition, urbanization and pollution have also been implicated in the overall increase in cancer incidence. Non-modifiable risks factors include inflammatory bowel disease and family history of CRC in first degree relatives.[5]

DETECTION

Screening for colorectal cancer aids in the early detection and treatment of early-stage CRC; which reduces mortality rates. In its updated guidelines published in 2002, the US preventative services task force (USPSTF) recommends that a CRC screening is performed for adults between the ages of 50-75 and those with a family history of CRC in a first degree relative; excluding those with specific inherited syndromes (the LS or FAP) and those with inflammatory bowel disease.[6]

The two recommended CRC screening methods are lower GI scope (colonoscopy and sigmoidoscopy); and fecal

occult blood testing. Additionally, it is considered that the risks and benefits of these screening methods vary.

Screening intervals: when to start and when to stop

For screening populations between 50-75 years of age, modeling evidence suggests that the population use any of the following three regimens: annual high-sensitivity faecal occult blood testing; sigmoidoscopy every 5 years combined with high-sensitivity faecal occult blood testing every 3 years, and screening colonoscopy at intervals of 10 years, will be approximately equally effective in life-years gained, assuming 100% adherence to the same regimen for that period.[7]

Lower GI scope (colonoscopy and flexible sigmoidoscopy)

Colonoscopy is not perfect despite being considered the golden standard reference in screening and early detection of CRC. Tandem studies in which patients are screened twice, once with a colonoscopy and then with CT colonography, showed that a colonoscopy could sometimes miss CRC and polyps, even those larger than 10 mm. In addition, colonoscopies are operator-dependent, which allows its sensitivity to be varied.[6] Risks from colonoscopy can vary from minor events like Diverticulitis to life-threatening events like major bleeding, bowel perforation and death.

Faecal occult blood

Adverse effects from high sensitivity stool tests: faecal immunochemical testing and SENSA were not addressed in any current studies. SENSA is a qualitative method that allows the blood, if present in stool, to form a highly conjugated blue quinone compound based on the oxidation of the guaiac by hydrogen peroxide to a blue-coloured compound.

Other recommendations

In March 2008, the American cancer society, the US multi-society task force on CRC and the American college of radiology unanimously recommended the following screening tools for CRC beginning at 50 years of age by:[7] high sensitivity fecal occult blood testing (FOBT) or fecal immunochemical testing annually; flexible sigmoidoscopy every 5 years; double-contrast barium enema every 5 years; CT colonography (virtual colonoscopy) every 5 years; colonoscopy every 10 years; and fecal DNA at an unspecified interval.

In July 2001, the Canadian task force on preventive health care concluded that for asymptomatic people, there was good evidence to support annual or biannual FOBT if no personal history of ulcerative colitis, polyps or colorectal cancer were present. Additionally, fair evidence to include flexible sigmoidoscopy in periodic health examinations of asymptomatic people older than 50 years of age.[8]

The American college of physicians, American academy of family physicians, American college of preventive medicine and centre for disease control and prevention have issued similar recommendations or endorsed the USPSTF recommendation.

RISK GROUPS

All screening recommendations in guidelines issued by different entities were established based on stratifying patients into 3 risk groups average, increased and high risk.

Those with no personal or family history in 1st degree relative of CRC or premalignant polyps were considered average risks and the recommendations for screening were based on the presence of symptoms. If an individual remained asymptomatic, screening by one of the previously mentioned methods should start at 50. Meanwhile, patients who experienced symptoms such as (melena, change in bowel habits and weight loss) should be evaluated for CRC at the time of symptoms.

Individuals with a personal history, family history in 1st degree relative younger than 60 or those with 2nd degree relative regardless of age of CRC or adenomatous polyps were considered increased risk groups.[9] The recommendations for those individuals involved screening them at an early age of 40 or 10 years before the age of diagnoses in the family member with colonoscopy repeated every 5 years, depending on the findings. On the other hand, if a personal history was absent, patients should be screened at the age of 40 with a repeat screening at intervals depending on the findings.[10]

High-risk groups included individuals with a strong and significant family history of CRC or polyps, those with high-risk medical condition including inflammatory bowel disease and patients that had an already established or highly suspected malignant bowel syndrome like FAP, LS, HNPCC and many others. Screening in high-risk groups must be initiated at a significantly younger age with shorter intervals when compared to other risk groups depending on the history of the given risk factor.

ASPIRIN AND CRC

Despite the significant role that screening had in reducing the mortality of CRC, it was facing important issues in terms of adherence and availability; thus, other more feasible, widespread and cost-effective methods were being studied in clinical trials and numerous COHORT studies. One that had been recently emerging was the use of low-dose aspirin to prevent CRC, primarily due to its major contributions in lowering cardiovascular disease (CVD). Considering that both CVD and CRC shared similar risk factors, the ability of aspirin to reduce the risk

of CRC had a strong appeal. A prospective mortality study which consisted of 662 male and 424 female adults enrolled in a cancer prevention study, showed that when aspirin was used at least 16 times per month was associated with a 40% reduced risk of colon cancer mortality over 6 years.[11] In a more recent updated analysis of this COHORT study, daily use of adult dose of aspirin (at least 325 mg) for at least 5 years was associated with a lower incidence of CRC compared with non-users (rate ratio [RR], 0.68; 95% [CI], 0.52-0.90), as well as reduced risks of other cancers like prostate (RR=0.81, 95% CI=0.70 to 0.94) and breast (RR=0.83, 95% CI=0.63 to 1.10).[12]

In 2007, the USPSTF recommended initiating low dose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a tenth or greater 10-year CVD risk, aren't at increased risk for bleeding, have an anticipation life expectancy of a minimum of 10 years and are willing to take daily low dose of aspirin for a minimum of 10 years.[13]

Polyps

Polyps are defined as usually benign, small growth with a stalk that protrudes from a mucous membrane. Polyps may develop a tendency to degenerate into cancer over a period of 5 to 15 years when it outgrows and starts invading the colonic wall. Thus, the methods used in CRC screening (colonoscopy) are also used and designed to remove suspicious polyps during examination before acquiring their invasive nature and transforming into a malignancy.

Factors contributing to polyps formation are similar to those considered for CRC and include age (50 or older), obesity, smoking, alcohol consumption and inflammatory bowel disease (ulcerative colitis and Crohn's) and personal or family history of colon polyps or colon cancer.

Polyps are classified according to their cancer transforming ability to neoplastic including adenomas and serrated polyps and non-neoplastic including hyperplastic polyps, inflammatory polyps and hamartomatous polyps.

Neoplastic polyps

Adenomatous polyps: An adenomatous polyp is a polyp that acquires a similar look to colonic mucosa when viewed and it can be benign but may acquire neoplastic features and malignant transformation.[14] According to their microscopic appearance and pattern of growth, adenomatous polyps are classified into 3 types.

Polyps with more than 75% longleaf or finger-like projections on their surface are known as villous polyps adenomas. Furthermore, 25% villous appearance made chiefly of glandular tissue is known as a tubular polyp and is the most encountered type with a prevalence of approximately 80%.[15] Known for their characteristic elliptical cigar-shaped dark purple grouped nuclei, goblet cells, loss or reduction that may not show dysplasia at first but will gradually develop dysplastic features and ultimately lead to CRC.[16] A tubulovillous polyp, as the name indicate, is a polyp with a mixture of both villous and tubular.

Serrated polyps: Named mainly after their saw-toothed appearance of the crypt epithelium, serrated polyps were formerly known as hyperplastic and were initially thought not to have any neoplastic abilities.[17] However, with developing imaging modalities and screening, serrated polyps are now categorized to hyperplastic, sessile serrated, and traditional adenomas based on their morphology and molecular profiles, each with its own risk of malignant transformation.

Sessile serrated lesions (SSL): Histologically are defined by irregular crypt distribution along with dilated serrated bases; crypts may be found branched extending horizontally and may be seen herniating through the muscularis mucosa. The terminology differs between the US, UK and the WHO regarding SSL diagnoses. WHO requires the presence of at least 3 crypts with minimum 2 crypts showing one or more of the features mentioned above, while the American gastroenterology association criteria involves the presence of a single crypt with the mentioned characteristic changes.[18]

Adenoma-carcinoma sequence is commonly known to explain the pathway of molecular changes. Ultimately, it leads to the malignant transformation of an adenoma. It is well known that more than 95% of colonic adenocarcinoma arises from polyps compared to a 0.2-11% risk of an adenoma turning into a malignant lesion.[19]

In the United States, the development of CRC is attributed to two main pathways, with the most common being the chromosomal instability (CIN) pathway, which counts for 80% of CRC. In this pathway, CRC develops from adenoma through a series of progressive mutations in numerous genes including K-ras, adenomatous polyposis coli (APC), P53 and SMAD4 leading to the development, formation and malignant progression of polyps. A germline or sporadic inactivation of the tumor suppressor gene APC starts the pathway, increasing the likelihood of developing a polyp. A mutation in K-ras follows, leading to the formation of the polyp and finally inactivation of p53 and the other tumor suppressor gene, along with an increased expression of COX accounts for the progression to carcinoma. Carcinomas that develop in this pathway are microsatellite stable (MSS) and mismatch repair proficient (MMR-P).[20]

When a methyl group (CH_3) is added to the cytosine nucleotide in a CpG dinucleotide context, this process is known as methylation. It is a physiological mechanism that regulates gene expression gene promotors without altering the DNA sequences. When important tumor

suppressors become silenced because of an atypical DNA methylation, neoplastic growths can be promoted. This bizarre methylation has been called the CpG island methylator phenotype (CIMP).[21]

The serrated pathway is the second less common pathway in which cancer develops through a malignant transformation of a SSL. As previously mentioned, sessile polyps were not considered to have any malignant transformation potential but with the use of CIMP marker panels, a molecular tool was provided to investigate the precursor lesions of CIMP+ tumors. When SSP's were investigated, many were found to be carrying BRAF mutation and were CIMP+ and when analyzed with an adjacent tumor segment was found to have shared features.[22]

Non-neoplastic polyps

With the increased use of colonoscopies, another group of polyps was identified and described; examples are those arising in solitary rectal ulcer syndrome, Hamartomatous polyps seen in PJS and JPS, incidental benign stromal polyps and systemic diseases associated polyps. In this report, Hamartomatous polyps were discussed.

PJS

Etiology and genetics

PJS is an autosomal dominant inherited disorder that develops as a result of a germline mutation in STK-11 tumor suppressor gene.[23] Characterized by mucocutaneous pigmentation and development of hamartomatous polyps that arises in intestinal and extra intestinal locations. Multiple studies provided various estimates of the prevalence of PJS and the widest prevalence range was 1 in 280,000 individuals. PJS was also a predisposing factor to multiple malignancies (gastrointestinal, lung, breast, gynecological and testicular cancers).[24]

Clinical features

Those affected by PJS developed hamaratamotaous polyps along their intestinal tract most commonly in the jejunum followed by the ileum, duodenum and the rest of the gastrointestinal tract in addition to other extra intestinal sites (renal pelvis, gallbladder, kidney, ureter). Flat, blue-gray to brown, 1-5 mm spots seen on the lips, buccal mucosa, eyes, nostrils and scantly seen on the fingers and soles of the feet and palms were the most common extra intestinal manifestation of PJS seen in 95% of the patients and were known as mucocutaneous hyperpigmentation and their degeneration to malignancy in considered rare. Other common presenting symptoms include rectal bleeding, anemia and small bowel obstruction, while some affected individuals can develop very subtle symptoms like abdominal pain and some will not develop any symptoms until later in life. The onset of intestinal symptoms was 13 years of age and 50% of those affected would had experienced symptoms by the age of 20.[25]

Diagnosis

PJS can be clinically diagnosed by the presence of 2 or more of the following features: 2 or more histopathological confirmed hamartomatous polyps in the small intestines, the characteristic mucocutaneous hyperpigmentation and/or family history of PJS.

Management

The diagnosis and treatment of small bowel hamartomas included the use of either two modalities intra-operative enteroscope (IOE), which was a combination of laparotomy (or laparoscopy) with endoscopy that ensured the entire visualization and polyp removal of the small bowel in an endoscopic or surgical manner and double-balloon enteroscopy (DBE) that consisted 200 cm enteroscopy and a 145 cm over-tube which had soft latex balloons at their tips used to grip the intestinal wall. At the same time, the endoscope can be inserted without forming redundant loops of the intestine each with its benefits and drawbacks.[26]

Screening recommendations

The main goal of screening was the early detection and complete removal of polyps that were >1 cm. Until now, there were no official screening guidelines for a patient with JPS, but the most newly published regimens did not differ. In general, for gastrointestinal tumors, it was recommended to screen with an upper endoscopy every 2-3 years, colonoscopy every 3 years starting at the age of 15 annually or every 2-3 years if polyps were not found. Females with JPS were recommended to have annual mammography and MRI imaging starting at the age of 25, a clinical breast examination every 6 months and an annual pelvic examination with a Pap smear by the age of 18. For testicular cancer an annual testicular examination should be commenced by the age of 10.[27]

JPS

Etiology and genetics

JPS is a rare autosomal dominant inherited disorder that develops due to gene mutation in BMPR1A or the SMAD4 gene, although a majority of those affected reported no family history and harbored the syndrome via a *de novo* pathway. JPS is characterized mainly by the presence of juvenile polyps in the gastrointestinal tract, most commonly the stomach, unlike JPS. The term juvenile refers to the histological type of the polyps noted, not the age group affected. Individuals diagnosed with JPS have an approximate 50% risk of gastrointestinal cancers.[28]

Clinical features

Individuals diagnosed with JPS often present with rectal bleeding and anemia, abdominal pain, diarrhea, prolapse and intussusception that usually start before the onset of puberty along with hamaratamotaous juvenile polyps found in their stomach and colon. Patients with confirmed SMAD4 gene mutation were found to have vascular malformations mucocutaneous telangiectasia and arteriovenous malformations and when noted concomitantly called Rendu-Osler-Weber syndrome or hereditary hemorrhagic telangiectasia (HHT).[29] Other clinical conditions include arterial aneurysms, mitral valve prolapse, skeletal and cranial abnormalities.

Diagnosis

The diagnosis of JPS depends on the clinical finding of at least the following criteria after other hamartomatous polyposis syndromes are ruled out: 5 or more juvenile polyps in the colorectal, multiple juvenile polyps anywhere along the gastrointestinal tract and or the presence of a family history of juvenile polyps regardless to the number.[30] Genetic testing for the affected genes (SMDA4 and BMPR1A) should also be considered for those who meet the clinical criteria to confirm the diagnosis and consul other family members at risk keeping in mind that not all patients with JPS will have a germline mutation.

Management and screening

Gastrointestinal polyps can be resected endoscopically, and for those with severe symptoms, more invasive surgical approaches can be implemented like colectomy and ileorectal anastomosis (IRA) or proctocolectomy. The same screening and surveillance recommendation from PJS applied.

CS

Etiology and genetics

The last hamartomatous polyp syndrome that will be covered in this article is CS. This rare autosomal dominant inherited disorder results from a mutation within the phosphatase and tensin homolog tumor suppressor gene (PTEN). PTEN mutation is not exclusively seen in CS but is also observed in other syndromes like Bannayan-Riley-Ruvalcaba syndrome (BRRS), which are also rare and known to cause hamartomatous polyps along the gastrointestinal tract. The reported prevalence of CS is 1 in 200000 and those affected are at high risk of developing breast, thyroid, and endometrial carcinoma.[31]

Clinical features

The most commonly experienced clinical feature of CS are the mucocutaneous lesions that includes *Trichilemmomas*, facial cutaneous facial papules, oral mucosal papillomatosis and other nonspecific symptoms like uterine fibroids, lipomas and hamartomatous polyps. Thyroid disorders have also been observed in CS, ranging from benign follicular adenoma or multinodular goiter to thyroid cancer. Breast cancer is the most common malignancy associated with CS with a lifetime risk of 25% to 50% for affected females.[32]

Diagnosis

The International cowden consortium developed the original diagnostic criteria later updated by the National comprehensive cancer network (NCCN) genetics/high-risk panel; the criteria include pathognomic, major and minor criteria.

Management

The management of CS is mainly aimed for symptomatic relief and cancer prevention or treatment. The aforementioned mucocutaneous manifestations of CS are benign treatment is warranted in case of complications or cosmetic unsatisfaction treating modalities can include topical agents, laser ablation, cryotherapy and sometime even surgical excision.[33]

FAMILIAL BOWEL CANCER: LS

Etiology

LS, formerly known as HNPCC, is one of the most common inherited bowel syndromes predisposing those affected to different malignancies most common being CRC and endometrial cancer (EC). Other cancer includes ovarian, small bowel, stomach and pancreatic cancers.[34] The lifetime risk of developing CRC in patients affected by LS is 3% and 1.8% lifetime risk of EC.[35] Recently the colon cancer family registry (CCFR), Win et al have estimated that the prevalence of LS among the general population was 0.35% which was considered high affecting 1 in every 279.[36]

Molecular pathogenesis and genetics

LS results from an autosomal dominant pathogenic defect in mismatch repair genes (MMR): 10-20% PMS2 and MSH6, 70-85% MLH1 and MSH2, respectively.[37] Mismatch repair genes are responsible for repairing DNA errors that accumulate in certain areas of repetitive DNA sequences found in the genome known as microsatellites. When mutations occur, it results in elongation or contraction of the microsatellite and this length discrepancy is known as microsatellite instability (MSI). MMR genes are usually responsible for repairing these errors. However, this process is impaired in Lynch syndrome, and thus, MSI is the standard genetic feature of LS and almost all LS resultant CRC shows MSI.[38]

Polymerase chain reaction (PCR) amplification is used to detect MSI by immune histochemical analysis of MMR proteins or specific repeats of genomic microsatellite If either test result is positive for loss of MSH2, MSH6 or PMS2, germline analysis is performed next to detect the absence of MLH1 warranting testing for MLH1 promoter hypermethylation and BRAF mutation, which would indicate sporadic MSI.[39]

Clinical features

The mean age for diagnosis of CRC in patients with lynch was 44-61 compared to 69 years of general population risk and was found more on the right side of the colon.[40] Patients affected complain of nonspecific gastrointestinal symptoms like abdominal pain, cramps, weight loss, anorexia, bleeding per rectum, hematochezia vomiting and altered bowel habit with risk of metachronous malignancy that increases with age. Muir-Torre syndrome is a variant of LS inherited in an autosomal dominant manner because of a germline MMR gene (usually MSH2 or MLH1) defect and is characterized by the presence of sebaceous adenomas and skin neoplasms.

Diagnosis

LS is considered a clinical challenge and is often mis-looked at due to the lack of taking full proper history and conducting a thorough physical examination.

Amsterdam I criteria or the less stringent Amsterdam II criteria is used after taking the patient history.[19] However, only 50% of affected patients meet these criteria, so the Bethesda guidelines were established to aid in identify patient that required MSI testing and more recent guidelines recommended testing all patients with CRC for MSI of MMR defects.

Amsterdam II criteria 1

The criteria were three or more relatives with histologically verified LS-associated cancer, one of whom was a first-degree relative of the other two; cancer involved at least two generations; one or more cancer cases diagnosed before 50 years of age.

Revised Bethesda guidelines 1

Diagnosis of CRC or endometrial cancer in a patient younger than 50 years of age; regardless of patient age, there was a presence of synchronous CRCs, metachronous colorectal cancers or other LS-associated tumors; diagnosis of CRC with a high frequency of microsatellite instability based on histologic findings (Crohn's-like lymphocytic reaction, mucinous or signet-ring cell differentiation or medullary growth pattern) in a patient younger than 60 years of age; diagnosis of CRC in one or more first-degree relatives with a LS-related tumor, with one of the diagnoses occurring before 50 years of age; diagnosis of CRC in two or more first- or second-degree relatives with LS-related tumors, regardless of patient age were the revised guidelines.

Patients diagnosed with LS must be screened annually with colonoscopy at ages 20-25 years. Females should be screened annually with bimanual pelvis examination and endometrial biopsies to detect and investigate endometrial thickening, polyps or masses and an annual transvaginal ultrasound starting at the age of 30 35. To detect gastric cancers, esophago-gastro-duodenoscopies must start at 30-35 and be repeated every 2-3 years.[41]

Treatment

The US multi-society task force (USMSTF) most recently published a guideline on treating CRC that recommended colectomy with ileorectal anastomosis as the primary procedure for patients diagnosed with LS and CRC with surveillances of the remaining colonic segment every 6 month to 1 year post operatively.[42]

The use of adjuvant chemotherapy with a regimen of FOLFOX or CAPOX (capecitabine and oxaliplatin) in patients with stage III (node-positive) colon cancer, irrespective of tumor mismatch repair status increased survival significantly longer among those with deficient MMR.[43]

Prophylactic total abdominal hysterectomy combined with bilateral salpingo-oophorectomy (TAH-BSO) was recommended for women who were 40 years and/or at the end of their childbearing years.

FAP

Etiology and genetics

FAP is another rare disorder that equally affects both sexes, with a variable reported prevalence in different countries. The latest was 1 in 11,300-37,600 by the European Union countries.[44] Moreover, 70% of FAP is caused by an autosomal dominantly inherited mutation in the tumor suppressor adenomatous polyposis gene (APC) found on the long arm of chromosome 5.[45]

Clinical features

Individuals affected usually start to experience nonspecific gastrointestinal symptoms such as abdominal pain, change in bowel habit, bleeding per rectum and weight loss during the second decade of life; a detailed physical examination can reveal the presence of hundreds of colonic polyps more common on the rectosigmoid part of the colon and those with untreated polyps will inevitably progress to CRC by the age of 35-40. Moreover, 90% of patients with FAP will develop gastric polyps noted in the duodenum 2nd and 3rd part with only 5% lifetime risk for malignant progression within 10 years. Lipomas, sebaceous cysts, epidermoid cysts and palpable osteomas are among the extraintestinal

symptoms experienced in patient with FAP. Adrenal, thyroid, pancreatic and the other cancers associated with FAP.[46]

Gardner syndrome, Turcot syndrome and attenuated FAP are three known variants of FAP diagnosed based on clinical manifestation. Gardner syndrome is characterized by the presence of both soft and hard tissues tumors like dermoid cysts, desmoids tumors, and osteomas) in addition to the adenomatous colonic polyps. Turcot, on the other hand, is associated with central nervous system tumors; attenuated FAP is the third attenuated variant of FAP, which is characterized by the presence of lesser polyps found at more proximal colonic locations and usually starts later in life.

Diagnosis

FAP is mainly clinical depending on the presence of the symptoms mentioned above, family history in addition to the presence of more than 100 polyps during imaging which is considered the most crucial sign of FAP according to international guidelines.[47] Investigations to diagnose and detect other extraintestinal manifestations should also be taken into consideration when FAP is suspected.

Treatment and surveillance

After establishing a confirmed diagnosis for FAP, considering the high, almost certain risk of CRC, surgery represents the preferred treatment modality for FAP patients. Surgical options vary and include total colectomy with ileorectal anastomosis (IRA), total proctocolectomy with ileostomy (TPI) and other procedures.[48] The timing of surgery depends on the severity of symptoms, age of presentation, number and the grade of dysplasia noted. Still, prophylactic surgery is preferred to reduce surgery-related postoperative morbidity and mortality. In addition, to choosing when to operate, screening must also be implemented when managing a patient with FAP to prevent the occurrence of CRC thus improve the chances of survival for those affected. According to the latest recommendation from the American Gastroenterological Association, screening with annual sigmoidoscopy starting at the age of 12 for those diagnosed with FAP carry the APC mutation or those with a known family history of FAP.[49] If results are normal, the time interval can be increased to every 2 years.[49] A patient that undergoes colectomy must be put on endoscopic surveillance at intervals of 6 months to 1 year.[51]

Chemoprevention

The use of NSAIDS like celecoxib (selective cyclo-oxygenase-2 inhibitor), rofecoxib and aspirin as a chemopreventive approach may cause regression of the adenomatous polyps in both size and number. However, due to their side effects and the need for long-term compliance, the use of these agents was not recommended and was not considered a substitute for surgery as CRC can develop in patients with FAP. Even polyps were suppressed by the effect of these pharmacological agents.[48,50]

CONCLUSION

Hereditary cancer syndromes should be considered an important factor in colorectal cancer. Diagnostic tools like faecal immunochemical tests and colonoscopy play an essential role. Timings of these tests should be performed at intervals as per guidelines. Screening tests will help early detect colorectal cancer and its management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Saeed MF, Ebrahim BM, Khairi SS, Varkey RG, Juma IM. Inherited bowel cancer: a review from a surgeon's perspective. Int J Community Med Public Health 2022;9:2709-17.