ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2022 April 15; 14(4): 748-946

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

Contents

Monthly Volume 14 Number 4 April 15, 2022

World Journal of Gastrointestinal Oncology

Monthly Volume 14 Number 4 April 15, 2022

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Hanlin L Wang, MD, PhD, Professor, Department of Pathology and Laboratory Medicine, University of California Los Angeles, David Geffen School of Medicine and Ronald Reagan UCLA Medical Center, Los Angeles, CA 90095, United States. hanlinwang@mednet.ucla.edu

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJGO* as 3.393; IF without journal self cites: 3.333; 5-year IF: 3.519; Journal Citation Indicator: 0.5; Ranking: 163 among 242 journals in oncology; Quartile category: Q3; Ranking: 60 among 92 journals in gastroenterology and hepatology; and Quartile category: Q3. The *WJGO*'s CiteScore for 2020 is 3.3 and Scopus CiteScore rank 2020: Gastroenterology is 70/136.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Ya-Juan Ma*.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
April 15, 2022

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Oncol 2022 April 15; 14(4): 833-841

DOI: 10.4251/wjgo.v14.i4.833

ISSN 1948-5204 (online)

MINIREVIEWS

Current guidelines in the surgical management of hereditary colorectal cancers

Shantata Kudchadkar, Safia Ahmed, Tanmoy Mukherjee, Jayesh Sagar

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Gao F, United States

Received: July 25, 2021
Peer-review started: July 25, 2021
First decision: October 3, 2021
Revised: October 16, 2021
Accepted: March 4, 2022
Article in press: March 4, 2022
Published online: April 15, 2022

Shantata Kudchadkar, Safia Ahmed, Tanmoy Mukherjee, Jayesh Sagar, Department of Colorectal Surgery, Luton & Dunstable University Hospital NHS Foundation Trust, Luton LU4 0DZ, United Kingdom

Corresponding author: Jayesh Sagar, FRCS (Ed), MBBS, MD, MS, Chief Doctor, Surgeon, Surgical Oncologist, Department of Colorectal Surgery, Luton & Dunstable University Hospital NHS Foundation Trust, Lewsey Road, Luton LU4 0DZ, United Kingdom.
jayesh.sagar@ldh.nhs.uk

Abstract

Incidence of colorectal cancer (CRC) is on rise. While approximately 70% of all CRC cases are sporadic in nature, 20%-25% have familial aggregation and only < 5% is hereditary in origin. Identification of individuals with hereditary predilection for CRC is critical, as it has an impact on their overall surgical management including surgical timing, approach & technique and determines the role of prophylactic surgery and outcome. This review highlights the concept of hereditary CRC, provides insight into its molecular basis, possibility of its application into clinical practice and emphasizes the current treatment strategies with surgical management, based on the available international guidelines.

Key Words: Colorectal cancer; Lynch syndrome; Familial adenomatosis polyposis; Immunohistochemistry; Metachronous colon cancer

Core Tip: Hereditary colorectal cancer, although contributes to only a small number of cases compared to sporadic cases, is significant due to its potential of carriage and also due to complexity in its management, considering possible involvement of cancers of other organs. We aim to look at the available evidence-based guidelines across the globe and attempt to summarize them together for readers to apply with simplicity.

Citation: Kudchadkar S, Ahmed S, Mukherjee T, Sagar J. Current guidelines in the surgical management of hereditary colorectal cancers. *World J Gastrointest Oncol* 2022; 14(4): 833-841
URL: https://www.wjgnet.com/1948-5204/full/v14/i4/833.htm
DOI: https://dx.doi.org/10.4251/wjgo.v14.i4.833

INTRODUCTION

Colorectal cancer (CRC) with a hereditary predisposition includes the most common form Lynch syndrome (LS) or hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP) with its two phenotypes (classic & attenuated)[1]. For each cancer case in the family, information on age at diagnosis, type of primary cancer, results of any cancer predisposition testing in any relative and family history should be updated periodically[2].

The diagnosis and accurate treatment of individuals with a hereditary component of CRC warrants a detailed knowledge of the primary syndrome and tumor genetics[2]. Immunohistochemistry (IHC) provides more information regarding the disease. The key concept of bowel cancer resection has to be obeyed in all CRC cases, irrespective of the type of mutation. Prime focus is on the oncological and functional outcome. The decision regarding the extended surgery should be based on the mutational status, gene, gender and the estimated individual risk. Minimal invasive surgery is the preferred surgical approach and post-operative quality of life should be the primary surgical outcome[3].

Guidelines from Association of Coloproctology of Great Britain & Ireland (ACPGBI) (2019), European Society for Medical Oncology (ESMO) along with the American Society of Clinical Oncology (ASCO) (2015) & Japanese Society for Cancer of the Colon and Rectum (JSCCR) (2020) for surveillance and management of both LS and FAP are complementary to each other[4-6] and elaborated further in this review.

HEREDITARY NON-POLYPOSIS CRC/LS

LS is characterized by autosomal dominant clustering of CRC and other extra-colonic cancers. It accounts for approximately 3%-5% of all CRC's and in the general population, approximately 1 out of 279 individuals has a pathogenetic mismatch repair (MMR) gene mutation[7].

HNPCC is also the most common predisposing hereditary cause of uterine cancer and is associated with the cancer of the stomach, ovaries and urinary tract (ureter, renal pelvis). The risk of development of LS associated tumors depends on multiple factors such as causative gene, type of mutation, environmental factors *etc*.[6]. HNPCC represents the clinical colorectal manifestation following the familial pattern of inheritance and LS is due to a germline mutation in one of the DNA genes MMR - mutL homolog 1 (MLH1), mutS homolog (MSH)2, MSH6 & PMS2. A change in one of these genes causes an accumulation of multiple errors in DNA repetitive sequences (microsatellites) along the genome[3]. This finding is known as microsatellite instability (MSI), and is frequent but not exclusive in LS. LS is usually associated with a high level of microsatellite instability, which carry a 50% risk of inheritance[8].

In order to identify LS patient, a detailed family history is necessary to confirm the fulfilment of the Amsterdam II and/or the revised Bethesda criteria[9]. Subsequent testing using IHC for MMR proteins, BRAF testing (a gene that encodes a cytoplasmic serine/threonine-protein kinase B-raf) for MLH1 loss of expression and MSI, is used to detect tumors lacking DNA MMR and plan comprehensive sequential testing[4]. Genetic counselling and genetic testing in a DNA sample in a normal tissue is crucial in every individual with a background of considerable family history and/or in those lacking MMR in the tumor specimen obtained during colonoscopy; and must be performed following consent[3].

Colon cancer in LS

Surgical management of LS patients should be individualized. Various factors play an important role when considering a surgical procedure; such as age at diagnosis, pre-existing co-morbidities, stage of the tumor, risks of metachronous colon cancer (MCC), surgical expertise, functional consequences of surgery and patient's wishes. LS patients have a considerable risk for development of metachronous CRC in any residual colorectum left behind, unlike patients with sporadic CRC. In some studies, the risk of metachronous CRC during follow-up is as high as 16% at 10 years[9]. Thus, expert opinion recommends extended resection - total abdominal colectomy (TAC) with ileo-rectal anastomosis (IRA). Life expectancy is increased by 2.3 years, when the procedure is performed in early years of life (before the age of 47), according to de Vos tot Nederveen Cappel *et al*[10]. Following an extended colectomy, decrease in the metachronous cancer risk must be balanced against the bowel functional expectations [11].

For LS patients, CRC risk varies according to the underlying genetic etiology. The lifetime risk is 30%-74% for MLH1, MSH2, and PMS2 mutation carriers, as compared to 10%-22% in MSH6 carriers[12]. In addition, from oncological point of view, there is insufficient evidence for LS patients with MSH6 or PMS2 mutations for advantage of extended colectomy over segmental resection[4]. On the other hand, despite yearly coloscopies, LS patients having MLH1 & MSH2 have a pronounced likelihood for developing metachronous CRC. Hence, in such cases a more extended surgery should be considered at the time of diagnosis.

Retrospective studies have shown the risk of developing a MCC after partial colectomy ranging from 11% to 45% over 8 to 13 years[13-15]. However, no prospective trials have been conducted to demonstrate a true survival benefit of TAC *vs* segmental resection[16]. Total abdominal hysterectomy and

bilateral salpingo-oophorectomy is recommended at the same time in LS patients, who have completed childbearing or are postmenopausal, to prevent the occurrence of endometrial/ovarian cancer[6].

A systematic review and meta-analysis by Malik *et al*[17] evaluated the risk of MCC and mortality in LS following segmental *vs* extensive colectomy. In this study, 1119 patients underwent segmental colectomies with an absolute risk of MCC in this group of 22.4% at the end of follow-up and 270 patients who had extensive colectomies had a MCC absolute risk of 4.7%. Segmental colectomy was significantly associated with an increased relative risk (RR) of MCC. RR after a segmental colectomy was 8.56 [95% confidence interval (CI): 3.37-21.73], as compared to 3.04 (95%CI: 1.46-6.34) in an extended colectomy in patients with a confirmed LS germline mutation and patients with LS diagnosis using the Amsterdam criteria. This study concluded five times greater risk of MCC after a segmental colectomy *vs* extensive colectomy in LS.

Rectal cancer in LS

Roughly 20% to 30% of LS patients will develop rectal cancer, with 15% to 24% of those with rectal cancer as their first presentation. Surgical options include a low anterior resection or abdomino-perineal resection, depending on sphincter involvement; or an extended resection with removal of all at-risk colorectum, *via* either a total proctocolectomy with an end ileostomy (TPC-EI) or more commonly a restorative ileal pouch-anal anastomosis (IPAA)[18,19].

The surgeon must consider various risk factors including possibility of metachronous colon cancer, bowel function, quality of life and co-morbidities of an individual, when determining the extent of bowel resection. A multidisciplinary team discussion including colorectal surgeons, gastroenterologists and pathologists is warranted to decide the best management plan for the patient, at the time of diagnosis of a colorectal primary[20].

International surveillance guidelines for LS

International surveillance guidelines for LS by ACPGBI United Kingdom[4], ESMO with ASCO[5], JSCCR[6] are summarized into pre-operative and post-operative as below.

Pre-operative: Starting age for surveillance colonoscopy should be based on the LS-associated gene[4].

Colonoscopic surveillance is recommended at a 2-yearly interval for all LS patients, starting from 25 years of age for MLH1 & MSH2 mutation carriers and 35 years for MSH6 & PMS2 mutation carriers[4].

Full germline genetic testing for LS should include DNA sequencing and large rearrangement analysis. Analysis of BRAF V600E mutation/ methylation of the MLH1 promoter should be carried out first to rule out a sporadic case, if loss of MLH1/PMS2 protein expression is observed in the tumor[5].

Germline mutation testing is indicated if tumor is MMR deficient and somatic BRAF mutation is not detected or MLH1 promoter methylation is not identified[5].

LS possibility should be individually evaluated in patients with suspicion of LS who have not yet diagnosed by genetic testing[6].

Surveillance of LS-associated tumors (in particular gynaecological, urological & gastrointestinal cancers) should be organized depending on the clinical and biochemical results (MSI/IHC). In LS patients with CRC, screening is suggested prior to elective colectomy[6].

Follow-up recommendations in mutation carriers include gynaecological examination on a yearly basis, in addition to the colonoscopy, starting from 30-35 years of age with 6 mo to 1 year interval. Surveillance methods include endometrial cytology & biopsy, CA 125 level and transvaginal ultrasonography[5,6].

In female LS carriers, risk reducing surgery with prophylactic hysterectomy and bilateral salpingo-oophorectomy can be considered as options, who have completed their childbearing for primary prevention of gynecologic cancer from age 35 onwards[5,6].

Upper gastrointestinal and urinary tract surveillance (urinalysis & cytology) should start at 30-35 years of age, at every 1-2 yearly interval.

Post-operative: Following surgery in LS patients with CRC, life-long surveillance with regular colonoscopy is recommended, due to the risk of possible development of MCC in the remaining colorectum[4,6].

Surveillance for recurrence of CRC following resection should be managed in a similar fashion to sporadic CRC[6].

Colorectal adenomas, when detected should be removed early, as they may progress to CRC in future [6].

Prophylaxis & chemoprevention: Prophylactic colectomy in LS patients (those with MMR mutation, but not developed CRC) is not currently recommended, partly due to the incomplete penetrance of the disease phenotype; as not all patients with a known gene mutation develop CRC[15]. Engel *et al*[21] stated that affected individuals have a 30% to 60% lifetime risk for developing CRC, depending on the underlying gene defect. Møller *et al*[22] conducted a multicentre study in patients with LS associated mutations affecting MLH1, MSH2, MSH6 or PMS2, which showed that collectively incidence of any cancer at 70 years is greater for all MMR gene mutation carriers, with a female predominance at 75% *vs* males at 58%. In MLH1 & MSH2 mutation carriers, malignancy was found from age 25 onwards as

compared to age 40 in MSH6 & PMS2 carriers. CRC cumulative incidence was high in MLH1 & MSH2 mutation carriers at 46% and 35% respectively; and lower in MSH6 & PMS2 mutation carriers at 20% and 10% respectively.

Indigo-carmine chromoendoscopy (CE) is recommended for the screening of LS patients, as compared to the white light endoscopy (WLE) by using optimal preparation, complete examination, and use of CE to reduce the cancer incidence. Various studies by Perrod *et al*[23], Lecomte *et al*[24], Hüneburg *et al*[25] and Hurlstone *et al*[26] reported a WLE adenoma miss-rate ranging between 52%-74%, thus demonstrating superiority of CE over WLE. Patient adherence to endoscopic follow-up programs can be improved by conducting dedicated educational workshops and creating support groups for LS to build motivation to join the program[27].

Recently conducted randomized trials did not characterize any protective effect of aspirin on CRC in a specific population. The CAPP2 trial did not show any aspirin protective effect on colorectal adenoma or cancer incidence after a mean of 29 mo, but a significant reduction in cancer incidence was observed at a mean of 56 mo[28]. Soualy *et al*[29] designed the AAS-Lynch trial to investigate whether the daily use of aspirin, at a dose of 100 or 300 mg, in LS patients under 75 years of age, would decrease the occurrence or recurrence of colorectal adenomas, compared with placebo. This is a prospective, multicentric, double-blind, placebo-controlled, randomized clinical trial and is estimated to be completed by year 2025.

FAP

The main characteristic feature of FAP is the development of hundreds to thousands of adenomas in the colorectum during second decade of life[30,31]. It is an autosomal dominant disease and accounts for less than 1% of all CRCs. It is caused by germline mutations in the tumor suppressor gene - defect in adenomatous polyposis coli (APC) on chromosome 22q21-22[32]. The expression of the disease may vary according to genotype and differ even within patients who share the same mutation due to modifying factors, such as gender[33].

Polyposis syndromes should typically be considered in patients with greater than 20 lifetime adenomas, patients with a personal history of desmoid tumor or other extra-colonic manifestations of FAP, or family members of individuals with known FAP, attenuated FAP (aFAP), or MYH-associated polyposis. Surgical management of FAP is complex and requires both accurate clinical judgment and technical skills. Treatment should include detailed counselling about the nature of the syndrome, its natural history, extra-colonic manifestations and the need for compliance with recommendations for management and surveillance[34].

The cornerstone of the management in FAP is prophylactic colorectal surgery due to 100% risk of CRC by 40 years of age if not treated early. Surgical decision-making, with regards to the timing of prophylactic surgery, extent of bowel resection and types of reconstruction, is influenced by both patient factors and disease characteristics[35].

The three main surgical options for FAP patients include subtotal colectomy with IRA, total proctocolectomy with/without mucosectomy & IPAA and TPC-EI. Table 1 describes indications, benefits and pitfalls of each of the surgical procedure. High ligation of the main blood supply to the bowel with removal of its mesentery form the principal basis of an oncologic bowel resection technique[31,36,37].

The follow-up strategy depends on the surgical procedure performed. Endoscopy should be done every 2-5 years when a pouch is constructed; whereas the interval should be 6 mo with total colectomy. In cases of pouch, a temporary diverting ileostomy may be fashioned to prevent anastomotic leakage[38,39]. Severity of polyposis determines the surgical decision of IRA *vs* IPAA - the more severe the polyposis, the greater the risk of metachronous rectal polyposis and/or rectal neoplasm.

aFAP: It represents a subset of patients who have germline APC mutation, with a diminished or "attenuated" colorectal phenotype. They possess < 100 synchronous colorectal adenomas and are not associated with complete penetrance of CRC. It is characterized by a later onset of colonic polyposis and later development of CRC (after 10-20 years) as compared to classical FAP. Most aFAP patients often undergo colectomy and IRA[42,43].

Minimal invasive surgical approach should be preferred for both forms of FAP. Currently, the standard surgical techniques for treatment of FAP include laparoscopic colectomy and proctocolectomy.

International surveillance guidelines for FAP

International surveillance guidelines for FAP by ACPGBI United Kingdom[4], ESMO with ASCO[5], JSCCR[6] are summarized into pre-operative and post-operative as below.

Pre-operative: Colonoscopic surveillance should usually start from 12-14 years of age in individuals genetically confirmed with a diagnosis of FAP. It is especially in at-risk individuals who have a first-degree relative with a clinical FAP, but absent APC mutation; which should be continued for 5 years, until a clinical diagnosis is reached and they are treated as FAP, or they can enrol in national bowel cancer screening programme when they reach the age[4].

Table 1 Comparing the three main surgical options in familial adenomatosis polyposis[6,30,39-41]

Surgical procedure	Indications	Benefits	Pitfalls
Ileo-rectal anastomosis	< 20 rectal, adenomas; < 1000 colonic, adenomas	Controls colonic polyposis. Better bowel function & good quality of life. Reduced risk of desmoid disease. Avoids stoma. Quicker recovery, especially useful in active teenagers	Risk of rectal cancer. Annual surveillance with proctoscopy & flexible sigmoidoscopy is required
Ileal pouch-anal anastomosis	< 20 rectal, adenomas; < 1000 colonic, adenomas	Removes nearly all polyps in colon & rectum. No need of permanent ileostomy. Quality of life is satisfactory	Increased complications. Unpredictable bowel function. Unpredictable quality of life. Possible need for ileostomy. Pouch complications: (1) Risk of pouch polyposis; and (2) Risk of cancer in anal transition zone. Surveillance is difficult
Proctocolectomy & end ileostomy	Low rectal cancer. When Ileal pouch-anal anastomosis is not indicated. Poor anal sphincter. Function	Complete removal of cancer risk in lower gastrointestinal tract	Permanent ileostomy. Sexual and fertility consequences such as dyspareunia, decrease in fertility, vaginal discharge in females and reduced libido, sexual satisfaction in males

Surveillance colonoscopy intervals may be individualized based on the colonic phenotype every 1-3 years[4]. An interval of 1-2 years is strongly recommended for patients with typical FAP and 2-3 years for patients with aFAP[6].

Germline genetic testing of APC and/or MUTYH should be considered for individuals with multiple colorectal adenomas (> 10). Full germline genetic testing of APC should include DNA sequencing and large rearrangement analysis[5].

The decision on the type of colorectal surgery in FAP patients depends on various factors including severity of rectal polyposis, risk of developing desmoids, mutation site in the APC gene and patient's age & wishes[5].

Search for extracolonic manifestations (gastroduodenal polyposis, thyroid cancer, desmoid tumors) in both variants (FAP and aFAP) is recommended, when colorectal polyposis is diagnosed or at the age of 25-30 years, whichever comes first[5].

Upper GI tract examination and monitoring should start at 25 years of age, every 6 mo to 5 years depending on the polyp burden[4].

Annual neck examination with ultrasound assessment for thyroid gland may be considered, starting at 25-30 years of age[5,6].

Counselling about the risk of formation of post-operative desmoid disease should be done for all FAP patients[4].

Annual abdominal examination and abdominal & pelvic computed tomography or magnetic resonance imaging every 3 yearly is recommended for patients with a family history of desmoid tumors [6].

Ophthalmology opinion and referral is needed in patients with a diagnosis of congenital hypertrophy retinal pigmentation epithelium (CHRPE). FAP screening, genetic testing and colonoscopy is advised in individuals with bilateral and multiple CHRPE lesions[4].

Colonoscopy should be carried out at every 2 yearly intervals, in families with aFAP, starting at the age of 18 to 20 years and continued lifelong in mutation carriers[5].

Post-operative: The cardinal factors influencing the timing of prophylactic proctocolectomy in candidates with FAP are as follows: (1) Total prevalence of colorectal malignancy; (2) Size, morphology & density of the adenomas; (3) Age at cancer occurence & death and presence/absence of desmoid tumors in family members; (4) Germline variant site in the APC gene; (5) Professional factors (educational, work & other environments of the patient); (6) Personal factors (fertility and presence/absence of male sexual dysfunction after IPAA); (7) Presence/absence of gastrointestinal symptoms; and (8) Histopathology of the tumor[6].

The definitive treatment of colorectal adenomas is proctocolectomy (prophylactic proctocolectomy) prior to the development of CRC[6].

Surveillance of the rectum should be carried out every 6 to 12 mo in cases with residual rectum and every 6 mo to 5 years in cases with ileo-anal pouch, depending on the polyp burden[5].

In FAP patients with locally advanced CRC, routine treatment for locally advanced CRC should be performed. The surgical procedure should be selected according to the condition of the FAP patients, if curative resection is possible[6].

Chemotherapy for CRC associated with FAP is similar to that used in sporadic cases[6].

In metastatic disease, treatment similar to that for metastases from sporadic CRC should be used, for curative resection group[6].

In FAP patients undergoing surgery for CRC, post-operative surveillance similar to that in sporadic CRC patients should be planned/performed[6].

Prophylaxis & chemoprevention: The most effective way of cancer prevention is to remove the colon and thus, the timing of prophylactic surgery should be considered, once the diagnosis is established. Severity of the polyposis decides the timing of surgery for patients diagnosed in their teenage years. Correct choice of the surgical procedure is the fundamental factor in reducing cancer risk, overall complications and sustaining a reasonable quality of life.

FAP patients undergoing prophylactic restorative proctocolectomy with IPAA are usually young and active. The frequency of bowel movements and faecal continence is of utmost importance, to have better quality of life. The continent function depends on the stool consistency, quality of sphincter muscles and pelvic nerves[3]. Transanal Total Mesorectal Excision is now a well-recognised surgical procedure in the treatment of mid and low rectal cancer, which involves a "bottom-top dissection" with improved visualization of the pelvic nerves and a rendezvous-approach[44].

Sulindac, a nonsteroidal anti-inflammatory agent, which inhibits cyclooxygenase enzyme (COX)-1 & 2, is the most tested drug in chemoprevention[45]. Lastly, care of FAP patients and their families is best given by centres of experience and excellence[46].

CONCLUSION

5%-10% of CRC cases are due to germline mutations, most of which are autosomal dominant with high penetrance. With accurate treatment, affected patients can benefit greatly when detected early in life. Thorough knowledge of the at-risk genetic mutations forms the cornerstone in formulating a precise treatment plan for patients with hereditary CRC. Syndromes with a 100% penetrance will require prophylactic surgery. In the treatment of every CRC, the basic concept of oncologic surgical procedure needs to be followed. Patient should be actively involved in the surgical decision-making. Lifelong follow-up is the predominant feature of the surgical treatment plan and every patient should be informed of the same well in advance. Improved patient adherence to the screening program is pivotal in surveillance.

FOOTNOTES

Author contributions: Kudchadkar S collected data and prepared the manuscript; Ahmed S and Mukherjee T analysed data; Sagar J reviewed and edited the manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Country/Territory of origin: United Kingdom

ORCID number: Shantata Kudchadkar 0000-0003-2637-5970; Safia Ahmed 0000-0003-2831-5314; Tanmoy Mukherjee 0000-0001-5571-5896; Jayesh Sagar 0000-0002-4242-101X.

Corresponding Author's Membership in Professional Societies: Association of Coloproctology of Great Britain and Ireland, ACP07354.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Wang JJ

REFERENCES

1 **Perea J**, Justo I, Alvaro E, Lomas M, Tasende JD, Marín JC, Franco A, Colina F, Rodríguez Y, Martínez J, Robles L, Urioste M, Hidalgo M. Surgical management of hereditary colorectal cancer: surgery based on molecular analysis and family history. *Rev Esp Enferm Dig* 2009; **101**: 536-540 [PMID: 19785492 DOI: 10.4321/s1130-01082009000800003]

2 **Kennelly RP**, Gryfe R, Winter DC. Familial colorectal cancer: Patient assessment, surveillance and surgical management. *Eur J Surg Oncol* 2017; **43**: 294-302 [PMID: 27546013 DOI: 10.1016/j.ejso.2016.07.008]

3 **Ambe PC**, Möslein G. Surgical management of hereditary colorectal cancer. *Mini-invasive Surg* 2018; **2**: 37 [DOI: 10.20517/2574-1225.2018.45]

4 **Monahan KJ**, Bradshaw N, Dolwani S, Desouza B, Dunlop MG, East JE, Ilyas M, Kaur A, Lalloo F, Latchford A, Rutter MD, Tomlinson I, Thomas HJW, Hill J; Hereditary CRC guidelines eDelphi consensus group. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCGG). *Gut* 2020; **69**: 411-444 [PMID: 31780574 DOI: 10.1136/gutjnl-2019-319915]

5 **Stoffel EM**, Mangu PB, Gruber SB, Hamilton SR, Kalady MF, Lau MW, Lu KH, Roach N, Limburg PJ; American Society of Clinical Oncology; European Society of Clinical Oncology. Hereditary colorectal cancer syndromes: American Society of Clinical Oncology Clinical Practice Guideline endorsement of the familial risk-colorectal cancer: European Society for Medical Oncology Clinical Practice Guidelines. *J Clin Oncol* 2015; **33**: 209-217 [PMID: 25452455 DOI: 10.1200/JCO.2014.58.1322]

6 **Tomita N**, Ishida H, Tanakaya K, Yamaguchi T, Kumamoto K, Tanaka T, Hinoi T, Miyakura Y, Hasegawa H, Takayama T, Ishikawa H, Nakajima T, Chino A, Shimodaira H, Hirasawa A, Nakayama Y, Sekine S, Tamura K, Akagi K, Kawasaki Y, Kobayashi H, Arai M, Itabashi M, Hashiguchi Y, Sugihara K; Japanese Society for Cancer of the Colon, Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2020 for the Clinical Practice of Hereditary Colorectal Cancer. *Int J Clin Oncol* 2021; **26**: 1353-1419 [PMID: 34185173 DOI: 10.1007/s10147-021-01881-4]

7 **Win AK**, Jenkins MA, Dowty JG, Antoniou AC, Lee A, Giles GG, Buchanan DD, Clendenning M, Rosty C, Ahnen DJ, Thibodeau SN, Casey G, Gallinger S, Le Marchand L, Haile RW, Potter JD, Zheng Y, Lindor NM, Newcomb PA, Hopper JL, MacInnis RJ. Prevalence and Penetrance of Major Genes and Polygenes for Colorectal Cancer. *Cancer Epidemiol Biomarkers Prev* 2017; **26**: 404-412 [PMID: 27799157 DOI: 10.1158/1055-9965.EPI-16-0693]

8 **Papadopoulos N**, Lindblom A. Molecular basis of HNPCC: mutations of MMR genes. *Hum Mutat* 1997; **10**: 89-99 [PMID: 9259192 DOI: 10.1002/(SICI)1098-1004(1997)10:2<89::AID-HUMU1>3.0.CO;2-H]

9 **Schneider R**, Schneider C, Büttner R, Reinacher-Schick A, Tannapfel A, Fürst A, Rüschoff J, Jakobeit C, Royer-Pokora B, Möslein G. [Colorectal Carcinoma with Suspected Lynch Syndrome: A Multidisciplinary Algorithm]. *Zentralbl Chir* 2015; **140**: 591-599 [PMID: 25372301 DOI: 10.1055/s-0034-1368480]

10 **de Vos tot Nederveen Cappel WH**, Nagengast FM, Griffioen G, Menko FH, Taal BG, Kleibeuker JH, Vasen HF. Surveillance for hereditary nonpolyposis colorectal cancer: a long-term study on 114 families. *Dis Colon Rectum* 2002; **45**: 1588-1594 [PMID: 12473880 DOI: 10.1007/s10350-004-7244-3]

11 **de Vos tot Nederveen Cappel WH**, Buskens E, van Duijvendijk P, Cats A, Menko FH, Griffioen G, Slors JF, Nagengast FM, Kleibeuker JH, Vasen HF. Decision analysis in the surgical treatment of colorectal cancer due to a mismatch repair gene defect. *Gut* 2003; **52**: 1752-1755 [PMID: 14633956 DOI: 10.1136/gut.52.12.1752]

12 **Giardiello FM**, Allen JI, Axilbund JE, Boland CR, Burke CA, Burt RW, Church JM, Dominitz JA, Johnson DA, Kaltenbach T, Levin TR, Lieberman DA, Robertson DJ, Syngal S, Rex DK. Guidelines on genetic evaluation and management of Lynch syndrome: a consensus statement by the US Multi-society Task Force on colorectal cancer. *Am J Gastroenterol* 2014; **109**: 1159-1179 [PMID: 25070057 DOI: 10.1038/ajg.2014.186]

13 **Barrow E**, Hill J, Evans DG. Cancer risk in Lynch Syndrome. *Fam Cancer* 2013; **12**: 229-240 [PMID: 23604856 DOI: 10.1007/s10689-013-9615-1]

14 **Natarajan N**, Watson P, Silva-Lopez E, Lynch HT. Comparison of extended colectomy and limited resection in patients with Lynch syndrome. *Dis Colon Rectum* 2010; **53**: 77-82 [PMID: 20010355 DOI: 10.1007/DCR.0b013e3181c702de]

15 **Parry S**, Win AK, Parry B, Macrae FA, Gurrin LC, Church JM, Baron JA, Giles GG, Leggett BA, Winship I, Lipton L, Young GP, Young JP, Lodge CJ, Southey MC, Newcomb PA, Le Marchand L, Haile RW, Lindor NM, Gallinger S, Hopper JL, Jenkins MA. Metachronous colorectal cancer risk for mismatch repair gene mutation carriers: the advantage of more extensive colon surgery. *Gut* 2011; **60**: 950-957 [PMID: 21193451 DOI: 10.1136/gut.2010.228056]

16 **Baucom RB**, Wise PE. Endoscopic and surgical management of hereditary nonpolyposis colorectal cancer. *Clin Colon Rectal Surg* 2012; **25**: 90-96 [PMID: 23730223 DOI: 10.1055/s-0032-1313779]

17 **Malik SS**, Lythgoe MP, McPhail M, Monahan KJ. Metachronous colorectal cancer following segmental or extended colectomy in Lynch syndrome: a systematic review and meta-analysis. *Fam Cancer* 2018; **17**: 557-564 [PMID: 29189962 DOI: 10.1007/s10689-017-0062-2]

18 **Kalady MF**, Lipman J, McGannon E, Church JM. Risk of colonic neoplasia after proctectomy for rectal cancer in hereditary nonpolyposis colorectal cancer. *Ann Surg* 2012; **255**: 1121-1125 [PMID: 22549751 DOI: 10.1097/SLA.0b013e3182565c0b]

19 **Möslein G**, Nelson H, Thibodeau S, Dozois RR. [Rectal carcinomas in HNPCC]. *Langenbecks Arch Chir Suppl Kongressbd* 1998; **115**: 1467-1469 [PMID: 9931914]

20 **Rodriguez-Bigas MA**, Möeslein G. Surgical treatment of hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome). *Fam Cancer* 2013; **12**: 295-300 [PMID: 23508345 DOI: 10.1007/s10689-013-9626-y]

21 **Engel C**, Vasen HF, Seppälä T, Aretz S, Bigirwamungu-Bargeman M, de Boer SY, Bucksch K, Büttner R, Holinski-Feder E, Holzapfel S, Hüneburg R, Jacobs MAJM, Järvinen H, Kloor M, von Knebel Doeberitz M, Koornstra JJ, van Kouwen M, Langers AM, van de Meeberg PC, Morak M, Möslein G, Nagengast FM, Pylvänäinen K, Rahner N, Renkonen-Sinisalo L, Sanduleanu S, Schackert HK, Schmiegel W, Schulmann K, Steinke-Lange V, Strassburg CP, Vecht J, Verhulst ML, de Vos Tot Nederveen Cappel W, Zachariae S, Mecklin JP, Loeffler M; German HNPCC Consortium, the Dutch Lynch Syndrome Collaborative Group, and the Finnish Lynch Syndrome Registry. No Difference in Colorectal Cancer Incidence or Stage at Detection by Colonoscopy Among 3 Countries With Different Lynch Syndrome Surveillance Policies. *Gastroenterology* 2018; **155**: 1400-1409.e2 [PMID: 30063918 DOI: 10.1053/j.gastro.2018.07.030]

22 **Møller P**, Seppälä T, Bernstein I, Holinski-Feder E, Sala P, Evans DG, Lindblom A, Macrae F, Blanco I, Sijmons R, Jeffries J, Vasen H, Burn J, Nakken S, Hovig E, Rødland EA, Tharmaratnam K, de Vos Tot Nederveen Cappel WH, Hill J, Wijnen J, Green K, Lalloo F, Sunde L, Mints M, Bertario L, Pineda M, Navarro M, Morak M, Renkonen-Sinisalo L, Frayling IM, Plazzer JP, Pylvanainen K, Sampson JR, Capella G, Mecklin JP, Möslein G; Mallorca Group (http://mallorca-group. eu). Cancer incidence and survival in Lynch syndrome patients receiving colonoscopic and gynaecological

surveillance: first report from the prospective Lynch syndrome database. *Gut* 2017; **66**: 464-472 [PMID: 26657901 DOI: 10.1136/gutjnl-2015-309675]

23 **Perrod G**, Samaha E, Rahmi G, Khater S, Abbes L, Savale C, Perkins G, Zaanan A, Chatellier G, Malamut G, Cellier C. Impact of an optimized colonoscopic screening program for patients with Lynch syndrome: 6-year results of a specialized French network. *Therap Adv Gastroenterol* 2018; **11**: 1756284818775058 [PMID: 29872454 DOI: 10.1177/1756284818775058]

24 **Lecomte T**, Cellier C, Meatchi T, Barbier JP, Cugnenc PH, Jian R, Laurent-Puig P, Landi B. Chromoendoscopic colonoscopy for detecting preneoplastic lesions in hereditary nonpolyposis colorectal cancer syndrome. *Clin Gastroenterol Hepatol* 2005; **3**: 897-902 [PMID: 16234028 DOI: 10.1016/s1542-3565(05)00403-9]

25 **Hüneburg R**, Lammert F, Rabe C, Rahner N, Kahl P, Büttner R, Propping P, Sauerbruch T, Lamberti C. Chromocolonoscopy detects more adenomas than white light colonoscopy or narrow band imaging colonoscopy in hereditary nonpolyposis colorectal cancer screening. *Endoscopy* 2009; **41**: 316-322 [PMID: 19340735 DOI: 10.1055/s-0028-1119628]

26 **Hurlstone DP**, Karajeh M, Cross SS, McAlindon ME, Brown S, Hunter MD, Sanders DS. The role of high-magnification-chromoscopic colonoscopy in hereditary nonpolyposis colorectal cancer screening: a prospective "back-to-back" endoscopic study. *Am J Gastroenterol* 2005; **100**: 2167-2173 [PMID: 16181364 DOI: 10.1111/j.1572-0241.2005.41481.x]

27 **Olivier R**, Randrian V, Tougeron D, Saurin JC. Endoscopy to Diagnose and Prevent Digestive Cancers in Lynch Syndrome. *Cancers (Basel)* 2021; **13** [PMID: 34298719 DOI: 10.3390/cancers13143505]

28 **Burn J**, Gerdes AM, Macrae F, Mecklin JP, Moeslein G, Olschwang S, Eccles D, Evans DG, Maher ER, Bertario L, Bisgaard ML, Dunlop MG, Ho JW, Hodgson SV, Lindblom A, Lubinski J, Morrison PJ, Murday V, Ramesar R, Side L, Scott RJ, Thomas HJ, Vasen HF, Barker G, Crawford G, Elliott F, Movahedi M, Pylvanainen K, Wijnen JT, Fodde R, Lynch HT, Mathers JC, Bishop DT; CAPP2 Investigators. Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. *Lancet* 2011; **378**: 2081-2087 [PMID: 22036019 DOI: 10.1016/S0140-6736(11)61049-0]

29 **Soualy A**, Deutsch D, Benallaoua M, Ait-Omar A, Mary F, Helfen S, Boubaya M, Levy V, Benamouzig R; AAS-Lynch group. Effect of chemoprevention by low-dose aspirin of new or recurrent colorectal adenomas in patients with Lynch syndrome (AAS-Lynch): study protocol for a multicenter, double-blind, placebo-controlled randomized controlled trial. *Trials* 2020; **21**: 764 [PMID: 32887653 DOI: 10.1186/s13063-020-04674-8]

30 **Bülow S**. Diagnosis of familial adenomatous polyposis. *World J Surg* 1991; **15**: 41-46 [PMID: 1847272 DOI: 10.1007/BF01658959]

31 **Half E**, Bercovich D, Rozen P. Familial adenomatous polyposis. *Orphanet J Rare Dis* 2009; **4**: 22 [PMID: 19822006 DOI: 10.1186/1750-1172-4-22]

32 **Aretz S**, Uhlhaas S, Sun Y, Pagenstecher C, Mangold E, Caspari R, Möslein G, Schulmann K, Propping P, Friedl W. Familial adenomatous polyposis: aberrant splicing due to missense or silent mutations in the APC gene. *Hum Mutat* 2004; **24**: 370-380 [PMID: 15459959 DOI: 10.1002/humu.20087]

33 **Lucci-Cordisco E**, Risio M, Venesio T, Genuardi M. The growing complexity of the intestinal polyposis syndromes. *Am J Med Genet A* 2013; **161A**: 2777-2787 [PMID: 24124059 DOI: 10.1002/ajmg.a.36253]

34 **Herzig D**, Hardiman K, Weiser M, You N, Paquette I, Feingold DL, Steele SR. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Inherited Polyposis Syndromes. *Dis Colon Rectum* 2017; **60**: 881-894 [PMID: 28796726 DOI: 10.1097/DCR.0000000000000912]

35 **Warrier SK**, Kalady MF. Familial adenomatous polyposis: challenges and pitfalls of surgical treatment. *Clin Colon Rectal Surg* 2012; **25**: 83-89 [PMID: 23730222 DOI: 10.1055/s-0032-1313778]

36 **Aziz O**, Athanasiou T, Fazio VW, Nicholls RJ, Darzi AW, Church J, Phillips RK, Tekkis PP. Meta-analysis of observational studies of ileorectal versus ileal pouch-anal anastomosis for familial adenomatous polyposis. *Br J Surg* 2006; **93**: 407-417 [PMID: 16511903 DOI: 10.1002/bjs.5276]

37 **Bülow C**, Vasen H, Järvinen H, Björk J, Bisgaard ML, Bülow S. Ileorectal anastomosis is appropriate for a subset of patients with familial adenomatous polyposis. *Gastroenterology* 2000; **119**: 1454-1460 [PMID: 11113066 DOI: 10.1053/gast.2000.20180]

38 **Al-Sukhni W**, Aronson M, Gallinger S. Hereditary colorectal cancer syndromes: familial adenomatous polyposis and lynch syndrome. *Surg Clin North Am* 2008; **88**: 819-844, vii [PMID: 18672142 DOI: 10.1016/j.suc.2008.04.012]

39 **Kartheuser A**, Stangherlin P, Brandt D, Remue C, Sempoux C. Restorative proctocolectomy and ileal pouch-anal anastomosis for familial adenomatous polyposis revisited. *Fam Cancer* 2006; **5**: 241-60; discussion 261 [PMID: 16998670 DOI: 10.1007/s10689-005-5672-4]

40 **Ziv Y**, Church JM, Oakley JR, McGannon E, Fazio VW. Surgery for the teenager with familial adenomatous polyposis: ileo-rectal anastomosis or restorative proctocolectomy? *Int J Colorectal Dis* 1995; **10**: 6-9 [PMID: 7745328 DOI: 10.1007/BF00337577]

41 **Yeo CJ**. Shackelford's Surgery of the Alimentary Tract, 2 Volume Set (Eighth Edition). In: Kalady MF, Boland CR, Church JM. Inherited Colorectal Cancer and the Genetics of Colorectal Cancer. Amsterdam: Elsevier, 2019: 1959-1980 [DOI: 10.1016/B978-0-323-40232-3.00165-5]

42 **Knudsen AL**, Bülow S, Tomlinson I, Möslein G, Heinimann K, Christensen IJ; AFAP Study Group. Attenuated familial adenomatous polyposis: results from an international collaborative study. *Colorectal Dis* 2010; **12**: e243-e249 [PMID: 20105204 DOI: 10.1111/j.1463-1318.2010.02218.x]

43 **Lynch HT**, Smyrk T, McGinn T, Lanspa S, Cavalieri J, Lynch J, Slominski-Castor S, Cayouette MC, Priluck I, Luce MC. Attenuated familial adenomatous polyposis (AFAP). A phenotypically and genotypically distinctive variant of FAP. *Cancer* 1995; **76**: 2427-2433 [PMID: 8625067 DOI: 10.1002/1097-0142(19951215)76:12<2427::aid-cncr2820761205>3.0.co;2-b]

44 **Monson JRT**, Arsalanizadeh R. Transanal Total Mesorectal Excision (TaTME) and Quality of Rectal Cancer Surgery: Do we Really Know? *Ann Surg* 2017; **266**: e88-e89 [PMID: 27070936 DOI: 10.1097/SLA.0000000000001736]

45 **Cruz-Correa M**, Hylind LM, Romans KE, Booker SV, Giardiello FM. Long-term treatment with sulindac in familial adenomatous polyposis: a prospective cohort study. *Gastroenterology* 2002; **122**: 641-645 [PMID: 11874996 DOI:

10.1053/gast.2002.31890]

46 **Vasen HF**, Velthuizen ME, Kleibeuker JH, Menko FH, Nagengast FM, Cats A, van der Meulen-de Jong AE, Breuning MH, Roukema AJ, van Leeuwen-Cornelisse I, de Vos Tot Nederveen Cappel WH, Wijnen JT. Hereditary cancer registries improve the care of patients with a genetic predisposition to cancer: contributions from the Dutch Lynch syndrome registry. *Fam Cancer* 2016; **15**: 429-435 [PMID: 26973060 DOI: 10.1007/s10689-016-9897-1]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com