# Efficacy, functional outcome and post-operative complications of total abdominal colectomy with ileorectal anastomosis vs. segmental colectomy in hereditary non-polyposis colorectal cancer

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**Abstract.** The primary objective of the present study was to compare the choice of colectomy, i.e. total vs. segmental colectomy, in cases of hereditary non-polyposis colorectal cancer (HNPCC/lynch syndrome), and to assess the efficacy, oncological safety, functional outcome and post-operative complications of total abdominal colectomy with ileorectal anastomosis vs. segmental colectomy in HNPCC. A total of 289 patients who fulfilled the Amsterdam I and II criteria for HNPCC were included in the present study. The criteria for confirmation of the diagnosis were five micro-satellite markers, namely BAT25, BAT26, D2s123, d5S346 and D17S250. Group 1 included those patients who received their diagnosis in the years 2011-2013 and those in group 2 had been diagnosed in the years 2014-2016. The cohort had been subjected to two different types of surgery: i) Standard and extended surgery including total colectomy with ileal pouch anal anastomosis and subtotal colectomy and ii) segmental resection of the colon. Analysis of patient data indicated that in group 1, the extended resection was performed more frequently than in group 2 (68 vs. 34% of cases) and accordingly, segmental resection was less frequent (32 vs. 66%; P<0.001). In conclusion, the extensive rather than the segmental resection has been commonly performed several years ago, but at present, the surgical method of choice in cases of lynch syndrome is segmental resection. Trial registry no. QU/MR2011/CRC5, dated 21 March 2011.

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## Introduction

To date, 'hereditary nonpolyposis colorectal cancer' (HNPCC) has remained to be fully defined with unified criteria. However, HNPCCs have various features in common, including an autosomal pattern of inheritance with 90% penetrance level, early age of onset, the proximal colon as the most common location, synchronous and metachronous colorectal cancers (CRS) and an increased risk for extra-colonic tumors. The most common pathological features of HNPCC include poor differentiation of cells, dysplasia, increased signet ring cells, massive tumor-infiltrating lymphocytes, a high frequency of microsatellite instability (MSI-H), loss of expression of DNA mismatch repair (MMR) proteins on immunohistochemistry and a germline mutation in one of the MMR genes (1).

HNPCC is also known as Lynch syndrome. Basically, it is a condition with an inherited tendency to develop CRC. The term 'no polyposis' indicates that this tumor occurs when no or only few polyps are present (2,3). In individuals that have already had colon cancer, but still have a remaining colon, the risk of developing another colon cancer is up to 60%. HNPCC is considered the most common hereditary CRC type, accounting for 2-6% of CRC cases worldwide (4-6). The basic pathology of Lynch syndrome lies in germline mutations in MMR genes. The basic four genes involved in the pathology of Lynch syndrome are mutL homolog 1 (MLH1), PMS1 homolog 2, mismatch repair system component (PMS2), mutS homolog 2(MSH2) and MSH6 (7).

The Amsterdam criteria I and II are recognized by the majority of researchers as the basic clinical criteria to identify hereditary Lynch syndrome in affected pedigrees (8-10). A molecular diagnostic test has been developed on the basis of knowledge gathered from molecular genetic studies. Furthermore, a microsatellite I instability test and immunohistochemical analysis are performed to assess the pathological and genetic aspects of HNPCC. It has been suggested that wide screening programmes should be performed to diagnose this syndrome at the early stage (9,10). High-risk individuals should be screened as soon as possible so that the development and progression of this tumor type is prevented.

The Amsterdam I criteria include the following clinical presentation specifically for Lynch syndrome: i) A minimum of three cases in one family who have been diagnosed with CRC, and at least one of them should be a first-degree relative; ii) occurrence of CRC in at least two consecutive generations; iii) histopathologically confirmed CRC occurring below the age of 50 years; iv) familial adenomatous polyposis should be excluded (Table I) (9,10).

The International Collaborative Group on HNPCC (ICG-HNPCC) introduced the novel Amsterdam II criteria that include cancers other than CRC in Lynch syndrome (Table I) (9,10).

HNPCC is inherited in an autosomal dominant manner. Unlike the diffuse polyposis observed in other hereditary colon cancer syndromes, patients with Lynch syndrome have a small and finite number of polyps (n<10), which are usually located in the right colon, and cannot be endoscopically differentiated from sporadic colon polyps. Those polyp cases in which pedigree is affected by lynch syndrome has more probability to progress into the malignant stage when comparison was done with the normal individual having the polyp. Recent studies have suggested a median age of CRC diagnosis of 61.2 years and a lifetime CRC risk of 52.2% in women and 68.7% in men (9,10). In HNPCC, metachronous and synchronous tumors are frequently observed. Histologically, the tumors are characterized by massive lymphocyte infiltration, a medullary growth pattern and a mucinous or signet ring cell differentiation. At present, the Bethesda criteria are used in the clinic, which are considered to be more appropriate than the Amsterdam criteria by certain clinicians, as those criteria include the MSI status together with the clinical results to diagnose HNPCC (Table I) (9,10).

HNPCC mostly affects the proximal part of the colon in 70% of cases and in the remaining 30%, its localization is sporadic. According to our observation, HNPCC occurring in younger patients (age, <45 years) tends to involve the proximal areas and sporadic areas in older patients (age >65 years) (11,12). The average age of Lynch syndrome-associated CRC manifestation is 45 years, which is~20 years lower than in the sporadic counterpart (11,12). A study by Lindor *et al* (13) reported that >40% of HNPCCs were located on the proximal areas rather than having a sporadic location.

Colonoscopy screenings have been recommended for mutation carriers to prevent the development and progression of cancer through early detection. Over a period of 3 years, Järvinen *et al* (14) observed that the screening for HNPCC in high-risk individuals decreased the incidence of CRC (6% in screened population as compared with 16% in the controls) and also decreased the mortality rate of HNPCC patients to 8% in the screened group vs. 22% in the control subjects.

The treatment of choice for HNPCC is surgical management, which includes either total abdominal colectomy (TAC), subtotal colectomy and segmental resection (14,15). At present, there is controversy over whether total or segmental colectomy is the best treatment for HNPCC (14,15). It has been suggested that prophylactic TAC is indicated in cases in which the frequency of CRC is high, as it is challenging to stop the spread of this tumor type to the advanced stage due to massive tumor growth. The decision to perform a prophylactic TAC should be based on a prior colonoscopy examination to investigate the spread of the tumor (15).

In patients with Lynch syndrome, the entire colonic mucosa is unstable and at risk of developing dysplasia and cancer, and a high incidence of synchronous and metachronous lesions is encountered (14). Therefore, the optimal surgical management of CRC in patients with an established diagnosis of Lynch syndrome usually requires a more extended approach than that in patients with CRC that do not exhibit lynch syndrome. It is therefore essential to pre-operatively identify Lynch syndrome when a patient is newly diagnosed with CRC. The most important factors that are indicative of the presence of Lynch syndrome are the patient's age and family history. The suspicion of Lynch syndrome should be raised when CRC occurs in a young person (<45 years), in the case of a family history of CRC, or when a patient develops multiple primary Lynch syndrome-associated cancer lesions. Internationally recognized guidelines, including the abovementioned Bethesda guidelines, were established to facilitate the identification of potential cases of Lynch syndrome during CRC screening (14). Historically, the revised Bethesda criteria have been the most frequently used guidelines, with the major indication for tumor MSI genetic testing being CRC diagnosis below the age of 50 years. However, it has been estimated that limiting tumor analysis to patients who fulfill the Bethesda criteria would lead to a failure to identify 28% of the cases of Lynch syndrome. Therefore, numerous institutions now routinely test all CRCs even in the absence of clinical high-risk features due to the high potential to identify Lynch syndrome (14). Syngal *et al* (15) assessed patients with hereditary gastrointestinal cancer syndromes that had received subtotal colectomy vs. those that received TAC and concluded that the choice of surgery was based on numerous factors, including risk due to family history, patient preferences, ease of screening and screening guidelines.

The primary objective of the present study was to compare the choice of colectomy, i.e., TAC vs. segmental colectomy, in cases of HNPCC in between 2011 and 2013 and between 2014 and 2016. The efficacy and oncological safety of TAC with ileorectal anastomosis vs. segmental colectomy in these HNPCC patients was assessed. In addition, patient satisfaction and post-operative complications were compared between HNPCC patients subjected to TAC with ileorectal anastomosis vs. those with segmental colectomy.

**Materials and methods**

*Patients*. The present study was approved by the Ethical Research Board of Weihai Second Municipal Hospital of Qingdao University (Weihai, China; trial registry no. QU/MR2011/CRC5). Written informed consent was obtained from each of the participants. A total of 289 patients who fulfilled the Amsterdam I and II criteria or HNPCC (16) were included in the study. The sample was selected according to the ICG-HNPCC rules and regulations (16), and furthermore, a Pedigree analysis of the 289 patients was performed, with an example presented in Fig. 1. Those patients for whom the Amsterdam criteria I and II were not fulfilled but genetic testing revealed germ cell mutations of MMR genes were also included in the total sample size.

Table I. AC-I and -II and Bethesda guidelines.

| Guideline | Criteria |
|---|---|
| AC-I | At least three relatives with histologically verified colorectal cancer:<br>1. One is a first-degree relative of the other two;<br>2. At least two successive generations affected;<br>3. At least one of the relatives with colorectal cancer diagnosed at <50 years of age;<br>4. FAP has been excluded. |
| AC-II | At least three relatives with a hereditary nonpolyposis colorectal cancer-associated cancer [colorectal cancer, endometrial, stomach, ovary, ureter/renal pelvis, brain, small bowel, hepatobiliary tract and skin (sebaceous tumors)]:<br>1. One is a first-degree relative of the other two;<br>2. At least two successive generations affected;<br>3. At least one of the syndrome-associated cancers should be diagnosed at <50 years of age;<br>4. FAP should be excluded in any colorectal cancer cases;<br>5. Tumors should be verified whenever possible. |
| Bethesda guidelines for testing of colorectal tumors for MSI | 1. Colorectal cancer diagnosed in a patient who is <50 years of age.<br>2. Presence of synchronous or metachronous colorectal, or other syndrome-associated tumors regard less of age.<br>3. Colorectal cancer with MSI-H histology diagnosed in a patient who is <60 years of age.<br>4. Colorectal cancer or syndrome-associated tumor diagnosed at an age of <50 years in at least one first-degree relative.<br>5. Colorectal cancer or syndrome-associated tumor diagnosed at any age in two first- or second-degree relatives. |

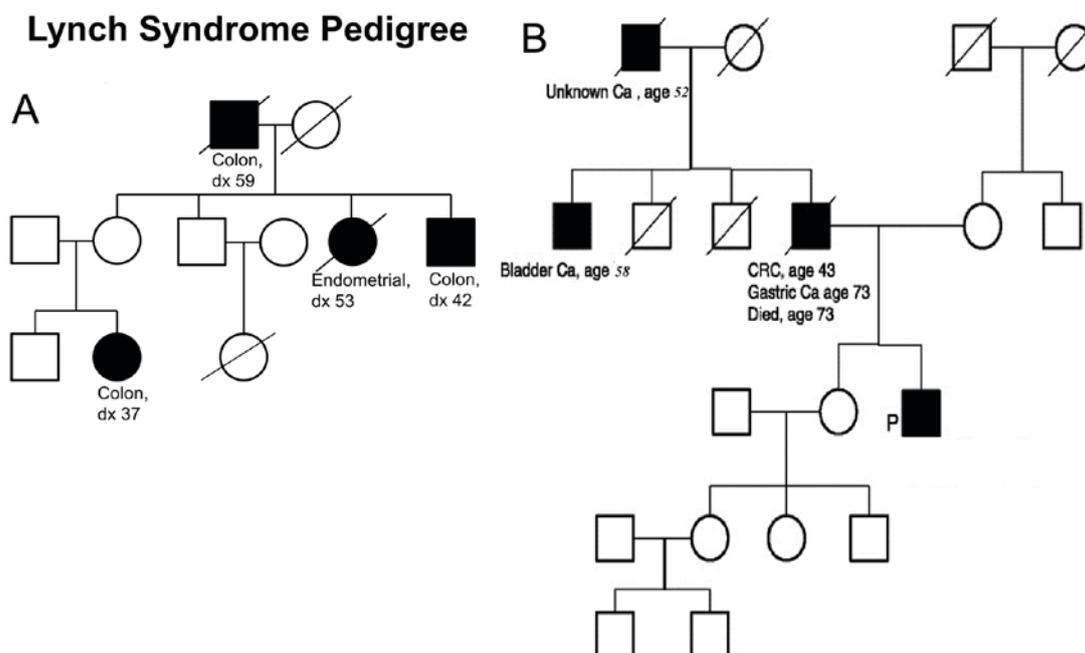AC, Amsterdam criteria; MSI-H, high microsatellite instability; FAP, familial adenomatous polyposis.



Figure 1. (A) Pedigree analysis of Lynch syndrome patients indicating that the syndrome may be transmitted through maternal or paternal lineages. (B) Pedigree of one family with autosomal dominant disease. Dx: Diagnosis Code, Ca: Carcinoma; Roman numerals, generation; Numbers, birth order; square, male; circle, female; shaded circle/square, individual possesses Lynch syndrome; non-shaded circle/square, individual does not possessed Lynch syndrome; half shaded circle/square, carrier of Lynch syndrome.

MSI testing was performed in all of the CRC patients (16). To confirm the diagnosis, five microsatellite markers, namely BAT25, BAT26, D2s123, d5S346 and D17S250 (16), were assessed as additional criteria (Fig. 2).
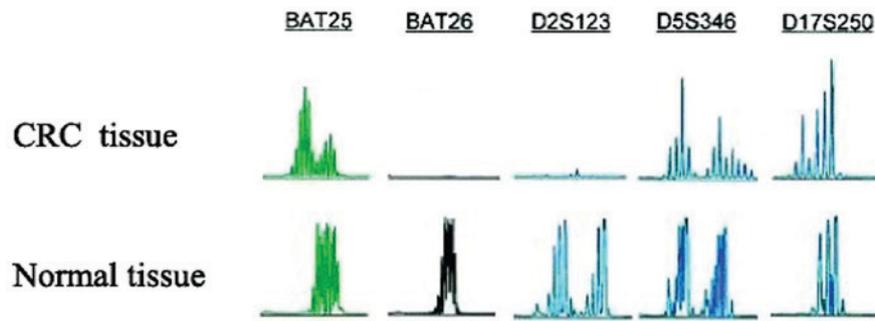
Figure 2. Micro-satellite instability testing for the five micro-satellites markers BAT25, BAT26, D2s123, d5S346 and D17S250. CRC, colorectal cancer.

The patient cohort comprised two groups: Patients in group 1 had received their diagnosis between 2011 and 2013, and Group 2 had been diagnosed between 2014 and 2016. The following two types of operation were applied in the present study: The standard and extended surgery was TAC with ileal pouch anal anastomosis (IPAA) and subtotal colectomy, and the second type of surgery was segmental resection of the colon, including hemicolectomy (right or left), resection (on the anterior part or on the lower anterior part) or Hartmann's operation. After the resection, the tumor sample was sent for histopathological examination

The Amsterdam criteria were used for the inclusion and exclusion of patients. Only CRC patients with familial adenomatous polyposis were excluded from the present study (16).

The age of patients was between 18 to 90 years; patients with ages of <18 years and >90 years were excluded from the present study.

*Surgical procedure of TAC with ileal anastomosis*. After the anesthesia, a small cut with the length of ~0.5 inches was made near the navel. The laparoscope was then inserted in to the abdomen through this incision and the mages captured by the laparoscope were displayed on the monitor. Once the laparoscope was in place, a total of 3-5 keyholes were made in the abdomen. The total number of incisions and their position depended on the physical build of the patient and difficulty level of the operation. The sigmoid colon and rectum were exposed, and subsequently, the colon was exposed and separated in various sections. The sections comprised the descending colon (left), the transverse colon, the ascending colon (right), the rectum and the sigmoid colon. Concurrently, the splenic and hepatic flexure were removed. Arteries that supplied blood to the colon were carefully preserved and kept separate. The ileal part was rejoined with the rectum. Subsequently, the colon was separated from the rectum and from the ileum to ultimately remove the colon. The surgical incision was then slightly expanded to pull the colon out of the abdominal cavity. The next step comprised the rejoining of the ileum and rectum. This rejoining process is known as Ileorectal anastomosis. A stapling technique was used for the anastomosis, and the abdominal cavity was then thoroughly rinsed and the anastomosis was checked for leakage. In the end, suturing of incisions was performed. Fig. 3 illustrates how the segmental resection was performed in the cases of Lynch syndrome.

*Follow-up*. All of the patients were followed up for 2.5 years. Each patient was reassessed following 3, 6 and 12 months up to 2.5 years.

*Assessment of oncological safety*. Recurrence of a histopathologically confirmed tumor at local areas on the ipsilateral side was considered to indicate poor outcome.

*Assessment of patient satisfaction after the surgery*. The Lowery scale was used for evaluation of patient satisfaction 6 months after surgery using a questionnaire. The scale ranges from 0 to 8 with 0 indicating poor and 8 excellent satisfaction.

*Analysis of functional outcome*. The functional outcome was evaluated 1 year following surgery and was based on the various aspects of bowel function. The items taken into account were the number of times the patients moved their bowels in one day, consistency of the stool, occurrence of gas, anorexia and incidence of perianal irritations. The data were collected with a questionnaire.

The gastrointestinal functional outcome (GIFO) scoring system was used for evaluation of bowel function (17). The effect of the patient age, length of follow-up, recurrence of CRC and whether the anastomosis technique was performed on the GIFO score was assessed.

*Statistical analysis*. SPSS version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. For categorical variables, the comparison was performed by using the chi square test/F-test (Fisher's exact test). For the analysis of continuous variables, Student's t-test was used. $P < 0.05$ was considered to indicate a statistically significant difference.

## Results

*Genetic testing*. Genetic analysis for Lynch syndrome was performed during the study period. Genetic evaluation of the genes MLH1, MSH2, MSH6 and PMS2 was performed in 200 out of 289 patients, and a germline mutation was detected in a total of 120 patients

Genetic testing also established germline mutations in the MMR genes in all of the 20 subjects who had a negative family history but fulfilled the other clinical diagnostic Amsterdam criteria I and II, and therefore, these subjects were also included in the population (7).
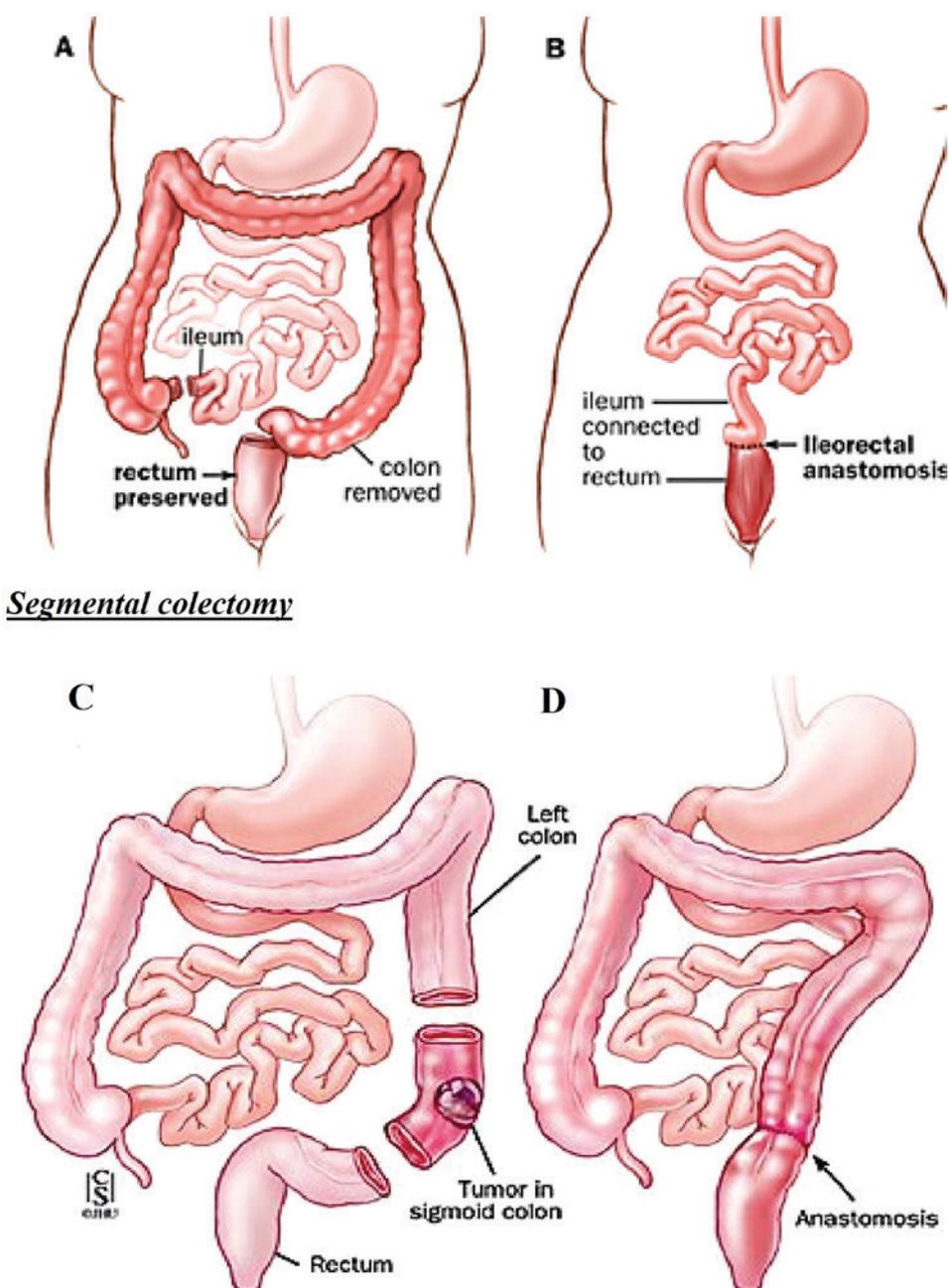
Figure 3. Schematic illustrating the method of total abdominal colectomy vs. segmental approach. (A) Total removal of colon with the preservation of the rectum. (B) Ileorectal anastomosis with connection of the ileum with the rectum. (C) Segmental correction, in which only the sigmoid colon has been removed, while the other parts of the colon had been preserved. (D) Segmental resection; anastomosis between the descending colon with the rectum.

*Patient characteristics.* Group 1 was comprised of 156 subjects and group II was comprised of 133 subjects. The mean age of the patients at the time of their diagnosis was 48 years (range, 18-90 years) in group I and 50.2 years in group II (range, 21-87 years). The gender ratio in the two groups was equal. The clinicopathological characteristics of the two groups are listed in Table II.

*Tumor location.* The most common location of Lynch syndrome lesions in the population of the present study was the proximal colon in each of the two groups, occurring in 62 cases (39.7%) of group 1 and 58 (43.6%) in group 2, followed by the distal colon, rectum and multiple locations. The extent of the disease at diagnosis in the Lynch syndrome patients

did not significantly differ between the two groups (P=0.186; Table II). The tumor cell differentiation status in the majority of Lynch syndrome cases was moderate in each of the two groups, followed by well- and poorly differentiated status. The number of subjects with well-differentiated status was 75 in group 1 and 68 in group 2 (Table II).

*Histopathological examination.* Lynch syndrome tumors demonstrated heterogeneity among poorly and well-differentiated carcinoma on histology. Immunohistochemical staining for the mismatch repair proteins MLH1, MSH2, MSH6 and PMS2 was performed. The results indicated that the expression of MSH2 and MSH6 mismatch repair proteins was retained in cancerous compared with tissues from

Table II. General clinical characteristics of the patient cohort.

| Variable | Group 1 (n=156) | Group 2 (n=133) | P-value |
|---|---|---|---|
| Median age (years) | 48 (18-90) | 50.2 (21-87) | 0.023 |
| Sex, no. of patients (%) | | | |
| Male | 97 (62.1) | 82 (61.6) | 0.40 |
| Female | 59 (37.9) | 51 (38.4) | |
| Location, no. of patients (%) | | | |
| Proximal colon | 62 (39.7) | 58 (43.6) | 0.07 |
| Distal colon | 48 (30.7) | 40 (30.3) | |
| Rectum | 38 (24.3) | 32 (24.0) | |
| Multiple | 8 (5.1) | 3 (92.2) | |
| Well Differentiated tumor status | 75 | 68 | |

Values are expressed as n (%) or the median (range). Groups: 1, diagnosis during 2011-2013; 2, diagnosis during 2014-2016.
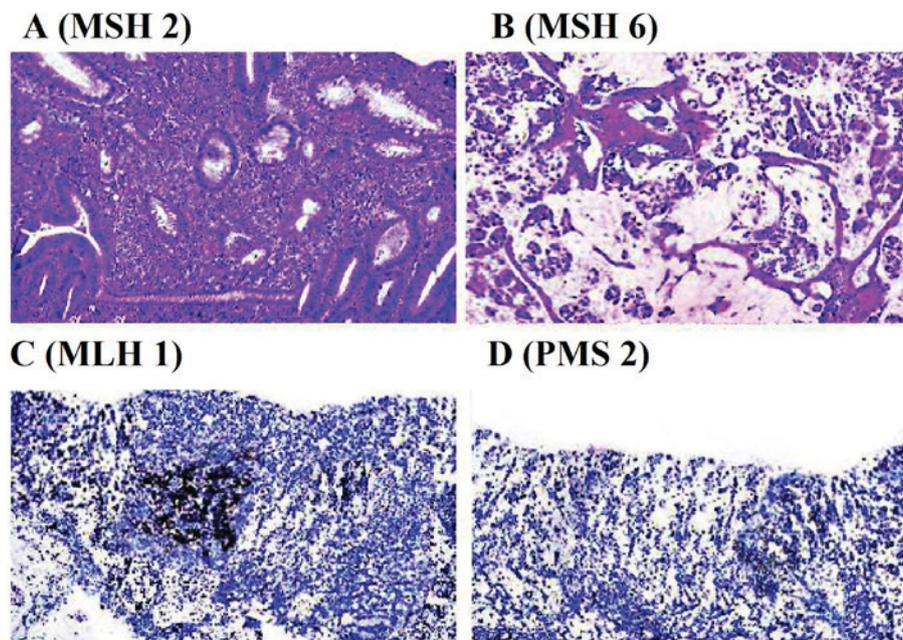


Figure 4. Immunohistochemical tumor testing for protein expression of the mismatch repair genes associated with Lynch syndrome, depicted for a single patient with colorectal cancer. Protein expression is preserved for (A) MSH2 and (B) MSH6, but absent for (C) MLH1 and (D) PMS2.Mayer's haematoxylin stain was used for counterstaining. Magnification, x400. MLH1, mutL homolog 1; PMS2, PMS1 homolog 2, mismatch repair system component; MSH2, mutS homolog 2.

patients without lynch syndrome. However, the expression of MLH1 and PMS2 was lost in cancerous compared with normal tissue (Fig. 4) (18).

The tumor-nodes-metastasis (TNM) stage in the majority of the patients was T2N2M0 (n=37 and 32 in group 1 and 2, respectively), followed by the T2N0M0 (n=32 and 31 in group 1 and 2, respectively).

*Surgeries*. In group 1, the extended resection was performed in 67.9% of cases; however, in group 2, only in 34% of cases received this surgery. Segmental resection was performed in 64.5% of cases in group 2 as compared with 32% in group 1; there was a significant difference in the rate at which each of the two types of surgery was performed between the two groups (P<0.001;

Table III). It was clearly demonstrated that previously (group 1), total abdominal colectomy was the surgery of choice in Lynch syndrome patients, while segmental resection was significantly preferred in group 2. (Table IV). The sites of the cancer occurrence were similar between the two groups, i.e. the proximal colon and distal colon. The present study indicated that the age of the patient is a major consideration for the choice of the surgery as, if the age of the patient is >60 years, the segmental resection was selected, and at an age of ≤60 years, total resection with ileorectal anastomosis was performed (Tables IV and V).

*Oncological safety*. In the patients subjected to TAC, a lower frequency of recurrence was recorded 1 year following surgery when compared with those that received segmental

Table III. TNM staging and oncological safety.

| TNM stage | Group 1 (n=156) | Type of surgery | Local recurrence | Group 2 (n=133) | Type of surgery | Local recurrence |
|---|---|---|---|---|---|---|
| Tis | 15 | | 0 | 13 | | 0 |
| TisN1 | 4 | | 0 | 2 | | 0 |
| T1N0 M0 | 28 | | 0 | 24 | Segmental correction | 4 |
| T1N1 M0 | 4 | | 0 | 4 | | 0 |
| T2N0 M0 | 32 | Segmental correction | 1 | 31 | Segmental correction | 3 |
| T2N1 M0 | 31 | TAC | 2 | 23 | TAC | 1 |
| T3N1 M0 | 2 | | 0 | 2 | TAC | 1 |
| T2N2M0 | 37 | Segmental correction | 5 | 32 | Segmental correction | 6 |
| T2N2 M1 | 3 | | 0 | 2 | | 0 |
| Total | 156 | | 8 | 133 | | 15 |

Groups: 1, diagnosis during 2011-2013; 2, diagnosis during 2014-2016. TAC, total abdominal colectomy; TNM, tumor-nodes-metastasis.

Table IV. Comparison of surgical methods between period 1 group and period 2 group.

| Operation type | Group 1 (n=156) | Group 2 (n=133) | P-value |
|---|---|---|---|
| Standard operation | 106 (67.5) | 46 (32.5) | <0.001 |
| Subtotal colectomy | 20 | 23 | |
| Total colectomy | 86 | 23 | |
| Segmental resection | 50 (32.0) | 87 (65.4) | <0.001 |
| Right hemicolectomy | 15 | 18 | |
| Transverse colectomy | 3 | 7 | |
| Left hemicolectomy | 2 | 8 | |
| Anterior resection | 1 | 27 | |
| Low anterior resection | 26 | 23 | |
| Ultralow anterior resection | 0 | 0 | |
| Hartmann's operation | 0 | 1 | |
| Abdominoperineal resection | 0 | 1 | |
| Segmental resection of colon | 3 | 1 | |

Values are expressed as n (%). Groups: 1, diagnosis during 2011-2013; 2, diagnosis during 2014-2016.

Table V. Factors affecting the surgical method.

| Variable | Standard operation | Segmental resection | P-value |
|---|---|---|---|
| Period | | | |
| Group 1 | 106 (67.9) | 50 (32) | 0.001 |
| Group 2 | 46 (34.5) | 87 (65.5) | |
| Location of CRC | | | |
| Proximal colon | 62 | 58 | - |
| Distal colon | 48 | 40 | |
| Age at diagnosis, years | | | |
| ≤60 | 130 (85.5) | 58 (42.3) | 0.002 |
| >60 | 12 (143.5) | 79 (57.6) | |

Values are expressed as n (%). CRC, colorectal cancer.

corrections; however, the difference was not statistically significant P>0.05 (Table III).

*Post-operative complications.* In the cohort of the present study, no mortalities occurred following 1 year of surgery, indicating oncological safety in each of the two groups and for each surgical method. However, the patients who received TAC had more complications than those subjected to segmental resection. Complications after TAC were noted in 27 patients in group 1 and in 13 patients in group 2. However, less complications were noted in each of the two the groups after the segmental resection (3 patients in group 1 and 5 patientsin group 2). The most common complication noted was intestinal obstruction, followed by intra-abdominal abscess. Out of the 34 patients with intestinal obstruction, this complication was managed with a conservative approach in 30 patients and with a surgical approach in only 4 patients (Table VI).

Table VI. Post-operative complications.

| Complication | Management | Occurrence | |
|---|---|---|---|
| | | Total abdominal correction group | Segmental correction group |
| Intestinal obstruction | Conservative (n=30) | Group 1 (n=20) | Group 1 (n=1) |
| | Surgical (n=4) | Group 2 (n=10) | Group 2 (n=3) |
| Intraabdominal abscess | Conservative | Group 1 (n=3) | Group 1 (n=1) |
| | | Group 2 (n=2) | Group 2 (n=1) |
| Wound infection | Conservative | Group 1 (n=1) | Group 1 (n=1) |
| | | Group 2 (n=1) | Group 2 (n=1) |
| Small bowel stump leakage | Conservative | Group 1 (n=1) | Group 1 (n=0) |
| | | Group 2 (n=0) | Group 2 (n=0) |
| Microperforation | Conservative | Group 1 (n=1) | Group 1 (n=0) |
| | | Group 2 (n=0) | Group 2 (n=0) |
| Anastomotic leakage | Conservative | Group 1 (n=1) | Group 1 (n=0) |
| | | Group 2 (n=0) | Group 2 (n=0) |

Groups: 1, diagnosis during 2011-2013; 2, diagnosis during 2014-2016.

Table VII. Aesthetic outcome rated by the patients.

| Lowery score | TAC (%) | Segmental correction (%) |
|---|---|---|
| Excellent (score 7-8) | 35.5 | 51.1 |
| Good (score 6-6.9) | 39.5 | 29.1 |
| Fair (score 5-5.9) | 20.8 | 19.8 |
| Poor (score <5) | 4.2 | 0.0 |
| Total | 152 (100) | 137 (100) |

TAC, total abdominal colectomy.

The long-term follow-up period was up to 12 months to monitor patients for post-operative complications. The most common complication was intestinal obstruction. In the present cohort, one patient presented with small-bowel leakage as a post-operative complication, which was further diagnosed as enterocutaneous fistula, and one patient presented with anastomosis stricture and micro-perforation; a surgical approach was used for the management of complications in these two patients (Table VI).

*Patients' satisfaction level following surgery.* Out of the 152 patients subjected to TAC, the cosmetic outcome was rated by 54 (35.5%), 60 (39.4%), 20 (25.0%) and 18 patients (11.2%), respectively. Of the 137 patients who had received segmental corrections, the above ratings of 4-1 were given by 70 (51.1%), 40 (29.2%), 27 (19.7%) and 0 patients (0.0%), respectively (Table VII).

*Functional outcome.* The functional outcome in the patients after the segmental approach revealed better results when compared with the total abdominal colectomy. The number of bowel movements per day in cases who had received the segmental approach was 4 vs. 6 in the TAC group (P<0.001). Regarding the items assessing rectal incontinence (e.g., soiling, particularly at night, incidental passive incontinence, perianal skin irritation, ability to distinguish between flatus and feces) (17), patients who had received segmental resection had significantly better results when compared with those who had received TAC. Between the two groups, no differences regarding anorexia and episodes of bowel discomfort were observed. The functional outcome measured with the GIFO score was significantly better for patients who had received segmental resection than for those subjected to TAC.

**Discussion**

At the time of surgical treatment of CRC, HNPCC patients frequently remain undiagnosed. Therefore, it is necessary to assess the detailed family history, hereditary factors and the past medical history. If Lynch syndrome is suspected, MSI analysis, immunohistochemistry and germline mutation analysis should be performed.

CRC has been considered the most common cancer type in numerous countries, including China. The rate has been continuously on the rise since the last 10 years. As CRC is known to have a familial predominance in the majority of instances, there is a high change and also a requirement to diagnose hereditary colorectal syndrome at the early stage (19,20). The diagnosis of Lynch syndrome at the early stages currently relies on standard screens for CRC in the majority of cases. Various studies and clinical trials suggested that registry-based screening is required to reduce the mortality rate of CRC in patients with Lynch syndrome (20,21).

Regarding best treatment option for HNPCC, extensive resection, including TAC and subtotal colectomy, has been the method of choice as compared with segmental resection, as the latter does not abrogate the high risk for synchronous CRCs.

A retrospective study by Win *et al* (21) from 2014 concluded that in patients who had received segmental correction of Lynch syndrome, the risk of metachronous colon cancer was 19 at 10 years, 47 at 20 years and 69% at 30 years. Various other studies also indicated that segmental resection was only performed in those cases in which total colectomy is not recommended. However, the choice of surgery in those cases varied from patient to patient, which was also reported by Rodriguez-Bigas and Möeslein (22). However, to date, no research study or clinical trial has concluded that extensive resection is a better treatment option than segmental resection. A study performed by Haanstra *et al* (23) revealed that in early stages of HNPCC, segmental resection or less extended surgery is better than TAC, as the 5-year survival rate was higher in the former group.

de Vos tot Nederveen Cappel *et al* (24) indicated that for young patients (age ≤27 years) with CRC and an MMR gene defect, TAC conferred a survival benefit of 2.3 years relative to segmental resection. However, the model used in the above study was severely limited by a failure to account for patient utility and quality-adjusted life years; their results only considered absolute survival. Furthermore, in the above study, total proctocolectomy and IPAA was a treatment strategy of choice due to the reduced occurrence rates of metachronous cancer, but it failed to consider the impact of IPAA on the quality of life (QOL).

You *et al* (25) examined the long-term bowel function and QOL after segmental resection, subtotal colectomy and TAC. They used validated survey methods, including a questionarre, to evaluate the QOL. Their results indicated that subtotal colectomy appears to represent a midpoint between TAC and segmental resection in terms of impairment of bowel function and QOL. However, the above study was retrospective and the patients who underwent each type of procedure exhibited a wide variation in terms of age, operative indication and pre-operative function. Subtotal colectomy may represent a compromise between the relative advantages of segmental resection and TAC, but the outcomes of this procedure in terms of QOL and metachronous occurrences of CRC require further study.

The present study also revealed that after segmental resection, the patients encountered less post-operative complications when compared with those that had received TAC, although this was not statistically significant. In addition, an improved overall QOL and an excellent patient satisfaction level was achieved for cosmetic and functional in the patients who received segmental resection when we compared with the patients with TAC and ileorectal anastomosis. However, with regard to oncological safety, the rate of recurrence in the patients subjected to TAC with ileorectal anastomosis was lower than that in the patients who had received segmental corrections; however, the difference was not significant. In order to assess if TAC is the best and safest procedure, a larger sample size with a longitudinal approach will be required for future study.

Natarajan *et al* (26) compared surgical management of Lynch syndrome using TAC with segmental resection and revealed that there was no significant difference in 5-year survival rate and overall survival between the patients that received the two different surgeries. Therefore, the present study recommends subtotal colectomy in patients with HNPCC.

Regarding the functional outcome the present study concluded that after TAC, the patients revealed more frequent bowel movements and rectal incontinence when compared with the segmental approach. However, a similar study performed in the Netherlands indicated a higher QOL and less post-operative complications in Lynch syndrome patients who underwent segmental resection when compared with those that had received TAC, with statistical significance (26).

In conclusion, the present study indicated that, the surgical method of choice in cases of Lynch syndrome is segmental resection. The study also suggested that the functional outcome of the segmental approach was better than that of TAC. However, the results of our study reveal that the oncological safety of TAC was higher than that of segmental resection. As a strategy for reducing the occurrence of HNPCC, a prompt nationwide effort to raise public awareness of hereditary CRC and an increased support for registries are required in China.

## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Authors' contributions

JS proposed the project, aims and objectives, and submitted the manuscript; MD calculated the results and XX collected the data, conducted statistical analysis and wrote the manuscript.

## Ethics approval and consent to participate

The present study was approved by the Ethical Research Board of Weihai Second Municipal Hospital of Qingdao University (Weihai, China; trial registry no. QU/MR2011/CRC5). Written informed consent was obtained from each of the participants. All methods were performed in accordance with the relevant guidelines and regulations as per the instructions of the Ethical Research Board.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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