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Total Colectomy with Subtotal Proctocolectomy of High Risk Colorectal Cancer Patients

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Abstract: ***Lynch syndrome is known by an early incidence colorectal cancer and comparatively common synchronous and metachronous neoplastic polyps or cancer or both. The aim of the current study to explore the beneficial of prophylactic colectomy in high risk patients with colorectal cancer. The medical records of 42 colorectal patients whom underwent surgery between 2006 and 2017 of the above hospitals diagnosed as colorectal cancer diseases were retrospectively reviewed. A Structured interview questionnaire was used. The questionnaire was including information on Socio- demographic data such as; age, gender, address, occupation and marital status. In addition, data on the presentation of the disease was obtained and data on complications and post-operative outcomes were also recorded. 42 patients were studied and the mean age ±SD of their age were 49.5± (10.2), 52.4% were male and 47.6% were female.76.1 % of the patients present with a bleeding per-rectum,71.4, 66.6, 61.9 present with abdominal pain, change in bowel habit and abdominal pain respectively. Abdominal mass and rectal mass were 11.9 and 9.5, the most common site of cancer was sigmoid, rectum and caecum 26.19, 14.3 and 11.9 respectively. The post-operative outcome was very less among patients, wound infection, seroma, incisional hernia and chest infection (7%, 7%, 4% and 4% respectively. We concluded from the current study that colorectal cancer with the technique of prophylactic total colectomy with or without subtotal proctectomy that increase the survival, decrease the morbidity and make the endoscopic follow –up easier and more comfortable to the patients for short and long follow-up interval.***

Keywords: colorectal cancer, total colectomy, subtotal proctectomy.

1. INTRODUCTION AND LITERATURE REVIEW

Lynch syndrome is a common inherited colorectal cancer liable syndrome and responsible for approximately 3 % of malignant colorectal cancers. Detailed family history and clinical evaluation are mandatory in finding peoples whom further assessment needed, through genetic counseling. finding the related germline mutations in mismatch repair genes in DNA will lead to more accurate assessment of colorectal and extra-colonic cancer risk [1]. Lynch syndrome is related to incidence of colorectal cancer in a younger age group and comparatively common synchronous and metachronous neoplastic polyps or cancer or both [2]. Peoples might have an incidence of 80 % higher colorectal cancer through their life [3]. Lynch syndrome is one of a well-known of autosomal dominant syndrome, that the family members being first degree relatives of an involve patient get a 50 % possibility of caring the mutated gene [4]. Moreover, the originator lesions have a tendency towards been flat rather been pedunculated which is usually located in the right proximal colon which is more difficult throughout colonoscopy [5]. This fact leads to the new growth of colorectal cancers in between planned follow-up up colonoscopy. Hence, most guiding principles recommend inspection colonoscopy every one to two years [6]. Lynch syndrome patients usually diagnose with a colorectal cancer between the age of 44–61 years [7, 8]. But, the incidence of colorectal cancer in younger age groups less than 20 years is rare, that the first screening colonoscopy should be done between the age 20–25 years and in families who have a member with a colorectal cancer due to lynch syndrome the first colonoscopy for screening should be done 10 years earlier than the affected family members [4]. Screening colonoscopy should be performed every two years up to the age 40, later on annually in the following years, colonic resection as a Prophylactic prouder to prevent future risk of colorectal cancer in highly risk patient should be done with evaluating the risk and benefit of the operation [9]. Prophylactic colectomy might be considered in rare circumstances and this should be discussed between the surgeon and the patient. One of the common criteria is Amsterdam I criteria which is designed to find families with a high risk of developing of colorectal cancer [10]. Another criteria is Amsterdam II , which is a revision of Amsterdam I criterial in 1999 in an attempt for increasing its sensitivity and extra colonic cancer [11]. Another guideline that involve some histological characters of HNPCC is The Bethesda's guidelines that guide for instability or liability of microsatellite as shown in (Table 1). Change from clinical diagnosis to genetic diagnosis begins 1993 as a mutation in mismatch repair gene [12, 7]. Mutations in EPCAM or MMR genes (PMS2, MSH6, MSH2, and

MLH1) is causative factor of developing colorectal cancer in lynch syndrome [13]. and this will be raised for those people who have increased family history or personal of colorectal neoplasia. There are high risk incidence association of extra-colonic cancer with Lynch syndrome such as; urinary epithelial (4– 5%), endometrial (40–60 %), hepato-pancreatic-biliary (2 to 7%), gastric (7 to 19 %), ovarian (9 to 13%), small bowel (1 to 4%), and CNS cancers (1-3%) [3, 8,14]. There are limited studies evaluating the value of prophylactic of colectomy in Lynch syndrome. Therefore, the aim of this study is to evaluate the value of prophylactic colectomy in high risk patients with lynch syndrome.

Table 1 : Bethesda guidelines [7]

Original	Revised
-Individuals with cancer in families that meet the Amsterdam criteria -Patients with two HNPCC-related cancers, including synchronous and metachronous colorectal cancer or associated extracolonic cancers -Patients with colorectal cancer and a first-degree relative with colorectal cancer and/or HNPCC-related extracolonic cancer and/ or a colorectal adenoma with one of the cancers diagnosed before age 45 years, and the adenoma diagnosed before age 40 years -Patients with right-sided colorectal cancer having an undifferentiated pattern on histopathologic diagnosis before age 45 years -Patients with signet-ring cell type colorectal cancer diagnosed before age 45 -Patients with adenomas diagnosed before age 40	-Colorectal cancer (CRC) diagnosed in a patient <50 -Presence of synchronous, metachronous colorectal or other HNPCC-associated tumors regardless of age -CRC with the MSI-H-like histology diagnosed in a patient less than 60 -CRC diagnosed in a patient with one or more 1st degree relatives with an HNPCC related tumor, with one of the cancers being diagnosed under age 50 -CRC in a patient with two or more 1st or 2nd degree relatives with HNPCC-related tumors, regardless of age

2. METHODS AND MATERIALS

The current study was carried out at three hospitals in Sulaimani city, international hospital, Shar hospital and Shorish hospital. In the current study, analysis of the data of 42 patients newly diagnosed to have colorectal carcinoma who were treated at Gastroenterology and Hepatology Teaching Hospital–Medical City from November 2006 to February 2017. The data were collected by a special form as below and the patients were admitted and treated at the surgical department where investigations carried out to prove the finding and determine the site and the extent of the disease include biochemical, endoscopy (upper and lower) and imaging as U/S ,CT, MRI and barium enema . Preoperative bowel preparation (mechanical using rectal enemas, oral polyethelinglycol solution (coloclean), antibiotics or both) was done for most of the patients presentating as an elective situation two days before surgery but not in case of emergency operations, fluid diet 72 hours prior to surgery. Prophylactic antibiotics (ceftriaxone 1 g plus metronidazole 500 mg intravenously) were given at induction of anaesthesia and continued for two days if no clinical feature of sepsis were present. We retrospectively reviewed the medical record of 42 patients whom underwent a surgery between 2006 and 2017. The surgical procedure (Total colectomy with subtotal proctectomy) was done for the patients. A written consent has been taken from patients, a structured questionnaire was applied to collect information regarding the patient's backgrounds and socio-demographical characteristics.

As a general principle for management for malignancy that the surgeon should obey the oncologic surgical rules as well as in colorectal cancer surgery for Lynch syndrome patients. Whether, the operation done through a laparoscopy or through traditional open technique, the surgeon should explore whole abdominal and pelvic cavity. For any second day involvement, a metastasis from colorectal cancer including liver, omentum, peritoneum, ovaries in pelvic peritoneum as well as the presents of malignant ascetic fluid. Oncologic rules are to obey non-touch technique tying the feeding vessels near the main vessels that supply the disease segment of the colon, a safety margin both proximal and distal to the lesion and mesenteric removal with the draining lymph-nodes and removal of any nearby involved if resection possible and looking for any synchronous liver metastasis whether it is possible to be resected in the same session or later on in a next look surgery take in to consideration time factors and morbidity , burden on the patients whether is the simple or a major resection , no matter the method of colonic anastomosis whether done by a stapler or by a hand sewn technique.

Data analysis

Data was collected and coded. The collected data were reviewed and analyzed using the Statistical Package for Social sciences (SPSS version 22). Descriptive statistics such as frequency and percentage was calculated. Measures of central tendency and dispersion around the mean were used to describe continuous variables. *P* value was obtained for the continuous variable using independent t test and was considered significant if it was less than 0.05.

3. RESULTS

Table 2 Characteristic of the patients with colorectal cancer.

Patients characteristic	**Total colectomy ± subtotal proctectomy**
Number of patients	42
Mean ±SD age (years)	49.5± (10.2)
Gender Male Female	 22 (52.4%) 20 (47.6%)
Address Inside city Outside city	 34 (80.9%) 8 (19.1%)
Marital Status Married Unmarried	 38 (90.5%) 4 (9.5%)
Previous surgery Colorectal cancer	8 (19.04%)

The current study included 42 patients with high risk colorectal cancer with total colectomy with or without

subtotal proctectomy. The mean ± SD of their age was 49.5± (10.2). 52.4% of the studied group were male and 47.6% were female. Most of our patients were from inside city 80.9% while a small of them were from outside 19.1%. 19.04 had a history of previous surgery of colorectal cancer (Table1).

Figure 1: Mode of presentation of colorectal cancer patients

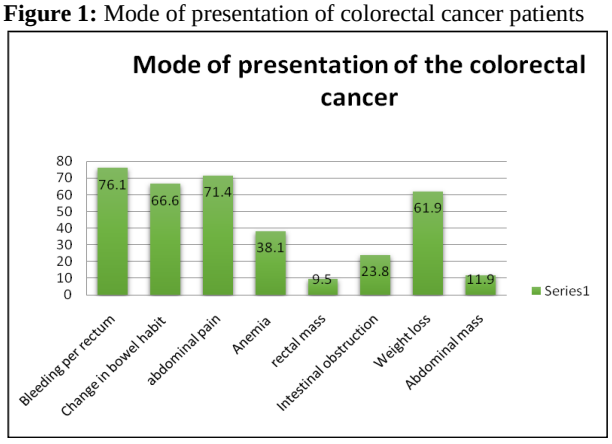

Figure 1 describes the mode of presentation of colorectal cancer. The highest percentage of our patients were presented with bleeding per-rectum, abdominal pain, change in bowel habit and weight loss (76.1, 71.4, 66.6 and 61.9) respectively. Whereas the lowest percentage were presented with anaemia, intestinal obstruction, abdominal mass and rectal mass (38.1, 23.8, 11.9 and 9.5) respectively.

Figure 2: Sites of colorectal cancer.

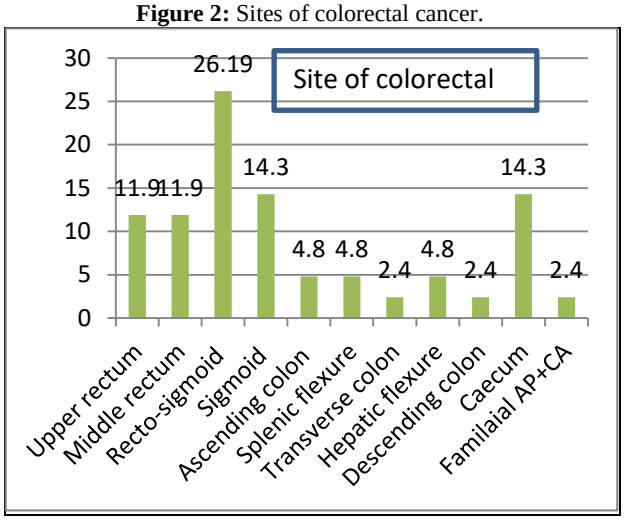

Figure 2 shows the sites of colorectal cancer. The highest percentage of cancer site were in recto-sigmoid, sigmoid, Caecum, upper rectum and middle rectum (26.19, 14.3, 14.3 11.9 and 11.9) respectively. Whereas the lowest percentages of cancer site were in descending colon, transverse colon, Splenic flexure and ascending colon (2.4,2.4, 4.8, and 4.8 respectively.

Table 2: distribution of preoperative Colonoscopic finding of colorectal cancer patients.

Preoperative Colonoscopic Finding	Total colectomy ±subtotal proctectomy
Synchronous polyp	15(35.71)
Failure to pass	6(14.29)
Ordinary with primary cancer	21 (50.0)

Table 2 shows the distribution of preoperative colonoscopic finding of colorectal cancer patients, most of our patients were had Synchronous polyp 35.17% and the other were had a failure to pass (14.29%). 50.0% of our patients were had a primary cancer with ordinary colonoscopy.

Table 3: Post-operative short and long term outcome.

short and long term morbidity	**Total colectomy ±subtotal proctectomy**
Patients comfortability	34 (80.95)
Discharge from hospital (early recovery)/ days	Median = 2
Post-operative pain and analgesia dose	Median = 2 dose
Early bowel motion / days	Median = 2
Frequency of bowel motion / day	Median = 4
Post-operative follow-up Colonoscopy(proctoscopy) /year/outpatient	Median = 1
Polyps formation \ 5years	Median =2
Time of operation	Median = 3hrs

Table 3 shows post-operative short and long term morbidity, most of our patients were comfortable post operation 80.9 %. Most of patients were discharge early from hospital with median of 2 days. The median of post-operative analgesic dose was 2, and the frequency of bowel motion was 4 motions per day. The median of 2 polyp formation were seen in our patients per 5 years, and the median of operation duration 3hrs.

Table 4: distribution of postoperative morbidity of colorectal cancer patients.

Morbidity	Total colectomy ± subtotal proctectomy
Chest infection	2(0.04)
Wound infection	3(0.07)
Seroma	3(0.07)
ileus	0 (0.0)
Incisional hernia	2(0.04)

Table 4 shows the distribution of postoperative morbidity of colorectal cancer patients, overall the post-operative complications were very low. However, a small percentage of complication were observed among patient's seroma, wound infection chest infection and inscional hernia (7%, 7%, 4% and 4% respectively).

4. DISCUSSION

Colorectal cancer still the commonest worldwide cancer in the gastrointestinal tract [15,16,17]. The ratio between male and female (M: F) is seen to be equal [18]. In this study, the (M: F) ratio is (1.1:1). In study by I. Palibrk et al the (M: F) ratio was 1.2:1 [19]. The commonest presenting symptom was bleeding per rectum in 76.1 % followed by change in bowel habit in 66.6% of our

patients, while the results of 2008, Waseem et al, bleeding per rectum in 63% followed by change in bowel habit in 55% [20]. Other study done in Iraq had showed 43.9% bleeding per rectum and 57.5% change in bowel habit [18,19]. Other symptoms were including pain, anemia, weight loss, abdominal mass and others. Multiple symptoms presented in 80% of our patients and it was single only in 20%. Most tumor were involving the distal part of the colon mainly the rectum, sigmoid and rectosegmoid junction (54%), nearly this is higher than many studies done worldwide like McCoy and Parks (U.K 1984) who reported 0.9% [20] and Smith et al(USA1989) who reported 4.8% [20]. while in Iraq 2008 Waseem had reported 17.5% [21, 22]. In our study the right colon in 22%, Shyamal Kumar Halder et al, found that the right colon is more commonly affected (33.3%) than left colon if we consider colonic cancer in isolation. If growths involving rectum, then rectum becomes the commonest site of affection in either age group [23]. Pre-existing factors were found only in 15 patients that have been analyzed, from these cases; polyps and villous adenoma presented with carcinoma account for (35.71%). Jarvinen et al found that ulcerative colitis represents 1.7% and FAP 0.6 %, also it is the same finding of other study done in Iraq 2001 [24]. The measures required to foster early detection of cases through proper methods for diagnosis are very vital. When there is suspicion of colorectal cancer, the most appropriate diagnostic tool is colonic-endoscopy for screening the whole as well as can perform biopsy of colonic lesion. The pitfalls of colonoscopy are an occasional incomplete examination of right colon 5-10% of cases, so completion barium enema some time is necessary [20], while Mc coy and Parks findings were 32% at rectum and sigmoid with 45% at splenic flexure and descending colon [20]. So, the tumors are more predominantly at the left side with recto-sigmoid predilection. In the present study, the post-operative complication was 23.8%, it is the same results of other study in Iraq [21]. Ashok Kumar et al had post-operative complications in (51.8%) [25]. The reason of surveillance in patients with HNPCC is to identify and get rid of precancerous growing polyps prior to development into malignant lesion. Therapeutic Colon endoscopy and polyp removal in HNPCC syndrome patients undoubtedly decrease the occurrence and fatality from colorectal cancer [26,27,28]. The usefulness of surveillance was evaluated in an attempt involving 40 families with Lynch syndrome over an eleven-year period. In a study found that screening colonic endoscopy for colorectal cancer at three-year interval period decrease the occurrence of colorectal cancer threat by 62 %, prevents colorectal cancer mortality, and cancer mortality by about 65 % in those family members [26]. In our study the prophylactic colectomy before detection of precancerous polyps or genetic determination of carrying the causative gene was reducing the risk of development of colorectal cancer in those cases that were not undergone colonoscopic surveillance at regular intervals. Our study shows the benefit of prophylactic colectomy in preventing the development of metachronous Colorectal Cancer While there are limited studies showing a survival advantages for total abdominal colectomy with illeorectal anastomosis, compared with segmental colectomy, the metachronous cancer risk in the remaining colon and mathematical assessment models favour the prophylactic colectomy. This approach showed increasing the life expectancy of 2.3 years by Markov decision model compared to segmental colectomy at 27 years of age [29]. A study was demonstrated the incidence of metachronous colon cancer in lynch syndrome after selective segmental colonic resection were 11– 45% in a follwup interval at 8- 13 years [30, 31, 32, 33]. Another study shows a higher incidence of new colonic cancer development after segmental colectomy to be as high as 72% at 40 years. Another study shows that patients having Amsterdam criteria have the chance of developing adenomas as high as 32% after segmental colonic resection [32] while in total abdominal colectomy with ilio-rectal anastomosis, whole or most the risky mucosa will be removed which by prevent the development of precancerous polyps but the remaining rectum should be screened annually as a clinic arrangement and rectal evacuation by an enema which decrease the incidence of metachronous rectal cancer during ongoing life as the risks shown in some studies to be between 3- 12% at 10 –12 years follow-up [4, 29, 34]. Quality of Life and Functional Outcomes are matters of consideration in patients with total abdominal colectomy with illeorectal anastomosis (TAC-IRA) as an alternative of a segmental colonic resection for cancer of colon in patients with Lynch syndrome. Removing the whole colon, a patient can be anticipated to have increased frequency and looser bowel motions than, when a selected right colectomy or sigmoid colectomy. The quality of life in patients with total abdominal colectomy with illeorectal anastomosis (TAC-IRA) compared to that after a more restricted segmental resection, there is a little data on those patients. A recent revision from the Netherlands particularly looking at this topic compared the quality of life of 43 Lynch syndrome patients who undergone a total abdominal colectomy with illeorectal anastomosis (TAC-IRA) with that of 51 Lynch syndrome patients who were treated with a restricted colonic excision, considering the life quality and bowel function questionnaires [27]. Life Quality as calculated by the Short Form-36 survey showed no significant difference. Analysis of the bowel Functional result questionnaire discovered that, after total Colonic resection, patients have an extensively elevated bowel motion frequency ($p<0.01$) and a considerably superior score on stool-related aspects ($p=0.06$) and social impact ($p=0.03$). The authors concluded that even though functional outcomes are poorer after subtotal or total colonic resection than after segmental colonic resection, generally, life quality does not vary in the two different surgical approaches in Lynch syndrome. Comparable outcome was also established in a smaller group study from the Cleveland Clinic presenting that frequent bowel motion was higher for patients with total resection of colon compared to segmental colonic resection (four bowel motion versus two bowel motions daily), but this was not associated with any change in continence for feces or flatus or on the whole quality of life [22]. Regarding the perioperative and postoperative morbidity and mortality, total abdominal colectomy with illeorectal anastomosis

(TAC-IRA) has been revealed to be a safe process with suitable outcomes even in the old aging patients [29,35]. A comparative study of perioperative morbidity and mortality of selective partial colonic resections with wider and extensive colectomy with ileo-sigmoid anastomosis or illeorectal anastomosis establish that mortality and morbidity (grade II/III) did not vary considerably between the two groups. On the other hand, the frequency of paralytic ileus postoperatively was greater in patients operated with more total resections [29]. Philosophy of the surgical approach, total abdominal colectomy with illeorectal anastomosis (TAC-IRA) must be considered in medically well patients with Lynch syndrome who is high risk to develop colorectal cancer [34]. This suggestion is depending on retrospective data and statistical analysis demonstrating the raised threat of metachronous colorectal cancer in these patients. In spite of these broadly accepted guidelines, the majority Lynch syndrome colorectal cancer in the USA is managed by local colonic resections [4, 29]. This divergence is mostly due to the deficit of a preoperative identification of Lynch syndrome or hereditary non-polyposis colorectal cancer (HNPCC). Regardless of the relative predominance of proximal colonic lesions in Lynch syndrome, cancer of the rectum is frequent; around 20 to 30 % of patients with Lynch syndrome will develop rectal cancer, including 15 to 24 % with rectal cancer as their index cancer [34, 36, 37, 38]. Rectal cancer associated with a higher risk with family history of rectal cancer of a first-degree relative [34]. The management of rectal cancer in Lynch syndrome is controversial; surgical procedures may be in the form of anterior resection of the rectum or low anterior resection or abdominoperineal proctosigmoidectomy, the choice of the procedure depends on whether the anal sphincter involved by the cancer or not or a more radical surgical resection, removing all of the colonic mucosa at risk in the form of a total proctocolectomy with terminal ileostomy or restorative ileal pouch-anal anastomosis. Segmental rectal resection alone with colorectal anastomosis achieves lower frequent bowel motions and normal anal sphincter continence and lower leakage than following an ileal pouch anal anastomosis [29]. Total proctocolectomy with ileal pouch anal anastomosis is a technically demanding surgery, need a specialized expert surgical team and carry important perioperative complications. Proctectomy leaves the whole colon at threat for the growth of metachronous colon cancer and demands a very hard yearly observation. Retrospective studies have established that in Lynch syndrome or HNPCC, the incidence of metachronous colon cancer following proctectomy is 15 to 54 % of patients [29, 39,40, 41, 42]. In a study from the Cleveland Clinic, 33 cases with HNPCC and an initial diagnosis of rectal cancer were managed with a rectal resection and regular colonoscopic follow up was done, five cases (15.2%) got metachronous adenocarcinoma at a median period of 6 years (range 3.5–16) following rectal resection, including three at advanced stage. in addition, another 36 % of cases got high-risk adenomas that were diagnosed through screening. Data from the Colon Cancer Family Registries found an elevated risk over time, with the risk of developing metachronous colon cancer being 19% at 10 years, 47% at 20 years, and 69% at 30 years after rectal resection [43]. The high incidence of metachronous cancer in Lynch syndrome or HNPCC; a total proctocolectomy with ileal pouch anal anastomosis must be fully discussed with patients diagnosed with rectal cancer. Radical excision for rectal cancer in Lynch syndrome is a controversial topic, and numerous factors involved in the decision making including the age of the patient, associated medical co-morbidities, stage of rectal cancer, preoperative anal sphincter continent and patient's agreement with meticulous follow up schedules must be taken into consideration [44].

5. CONCLUSION

This study was the first study in Kurdistan Region/Iraq, describing the high-risk patients with colorectal cancer with the technique of prophylactic total colectomy with or without subtotal proctectomy that increase the survival, decrease the morbidity and make the endoscopic follow –up easier and more comfortable to the patients for short and long term follow-up interval.

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