

Colorectal Cancer Survival at Dr. Orlando Smith Hospital, Tortola, BVI

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Abstract

Introduction: Colon cancer is the 4th leading cause of cancer deaths in the Caribbean, no study of colorectal cancer has been done previously on British Virgin Islands population, therefore there is limited data available on mortality and prevalence in this population. Our Multidisciplinary tumor board team was first established in 2016 and reviews all cancer patient at the Dr. Orland Smith Hospital, These Multidisciplinary tumor boards are intended to improve the outcomes of this group of patients. This is consistent with previous research in the UK by Mac Demid., *et al* [1] and Greece by Loannidis., *et al* [2]. In 2016 a systemic review by B. Pillay., *et al* [3] suggested that there was limited evidence that Multidisciplinary tumor board meetings resulted in improved patient outcomes. So how has Multidisciplinary tumor boards affected our patient outcomes at the Dr. Orlando Smith Hospital for colorectal cancer? Has there been any improvement in colorectal cancer survival?

Aim and Method: The aim of this study is to determine if there has been any difference in overall survival in colorectal cancer patients since the establishment of the Multidisciplinary tumor board at our principal referring hospital (Dr. Orlando Smith Hospital). A retrospective study was done reviewing all patients diagnosed with colorectal cancer from 2013 to 2019. Demographic, pathologic and treatment data were collected from the patients charts and electronic medical data base. All the pathology reports over this time period was also reviewed to capture all the patients with colorectal cancer. This data was then computed in excel and analyzed using SPSS. Additional data collected included, clinical presentation, screening, type of surgical management, postoperative complications and staging.

Results: 32 new patients were diagnosed with colorectal cancer over the 7-year period. The majority of patients presented late (stage 4) and a significant amount presented as intestinal obstruction requiring acute surgical care. The mean age at diagnosis was 70.2 years, 60% of patients were male, 43% had left sided tumors. Mortality was the same in both left and right sided tumors however 88% of rectal cancer patient died. 90% of patients had no screening done prior to diagnosis. overall survival time was 16.7 months. 63% of patients were discussed at multidisciplinary tumor boards. When a comparison was made between case discussed at multidisciplinary tumor boards and those who were not, there was no significance difference in the survival curve ($p = 0.600$).

Conclusion: The evidence does not support an improvement in patient overall survival in colorectal cancer after the implementation of the multidisciplinary tumor boards. There has been an increase in cases over the last 3 years, these cases present, with poor prognostic factors. The majority are stage 4 disease (43%), 23% presents as emergencies with intestinal obstruction, 50% have hypertension etc. Hence these patients have a decreased probability of overall survival even before being discussed at multidisciplinary tumor boards. A national screening program would definitely help in early detection and together with targeted care to British virgin island population, overall survival can be improved.

Keywords: Colorectal Cancer Survival; Orlando Smith Hospital; BVI

Abbreviations

ACG: American Collage of Gastroenterology; AJCC: American Joint Committee on Cancer; APR: Abdominal Perineal Resection; BSG: British Society of Gastroenterology; CAP: The College of American Pathologist; CDC: Centers for Disease Control and Prevention; CRC: Colorectal Cancer; DMMR: Deficient Mismatch Repair; EGFR: Epidermal Growth Factor; EUS: Endoscopic Ultrasound; FAP: Familial Adenomatous Polyposis; HNPCC: Hereditary Non-Polyposis Colorectal Cancer; H-MSI: High Frequency Microsatellite Instability; MSI: Microsatellite Instability; NHS: National Health Service; SES: socioeconomic status; TNM: tumor, node, metastasis; UICC: Union for International Cancer Control; VEGF: Vascular Endothelial Growth Factor

Aim

To determine if there is a difference in the survival of colorectal cancer patients that were discussed at MDT compared to those who were not discussed at MDT.

Objectives

1. To determine the demographics of our colorectal cancer population
2. To identify if patients are being screened for colorectal cancer prior to diagnosis
3. To determine most frequent presentation and most frequent type of colorectal cancer in our population.
4. To identify if patients are receiving adequate treatment according to recommended guidelines (surgical/ medical)
5. To determine stage at which these patients present the most at our hospital.
6. To identify the histopathological characteristics of our colorectal population.
7. To identify if we have increase rate of post op complications.

Method

This is a retrospective cohort study of patients diagnosed with colorectal cancer between January 2013 to December 2019 approximately 3yrs before and after the establishment of the MDT boards.

Data will be taken from available patients notes (physical charts and information from the electronic medical record from 'Cellma' software data base). Patient's personal identifications will not be recorded.

Histopathology reports will also be reviewed to ensure no patient is missed.

Inclusion criteria

1. All patients with a histopathological diagnosis of colorectal cancer from January 2013 to December 2019.

Exclusion criteria

1. Patients without a histological diagnosis of colorectal cancer.
2. Patients not discussed at tumor boards after August 2016.

3. Patients with other cancer of Gastrointestinal tract cancers (small intestines, stomach etc.)
4. Patients diagnosed before 2013 and after 2019.

Procedure

This project was first discussed with Dr. Elizabeth Dos Santos, clinical Oncologist and coordinator of MDT boards and given the green light.

The manager of the records department, Quality manager and CEO were then informed of the research project and no objections were made. Dr. Dos Santos assisted in informing the above-mentioned persons as well as the Pathologist (Dr. Redhead).

Codes for patients with cancer of colon/large intestine, cancer of rectum and cancer of rectum with colon cancer were then used to identify patients for this study by the staff at the records department. The charts identified (physical charts and electronic charts) were then reviewed for histopathology report confirming colorectal cancer, once this was done, a questionnaire (Appendix A 1) was used to extract data from each chart.

Records from the pathology department were also reviewed for patients with colorectal cancer as well as data from MDT boards to ensure no patient was missed.

The data was treated with strict confidentiality as it was only viewed in the records department and no patient identifiers were documented to identify specific patients.

Instrumentation

A questionnaire (Appendix A 1) consisting of 33 points was used to extract data from each of the patients accepted into the study. From these questions I was able to extract demographic data, stage, location of cancer, surgical and medical management of patient also patient survival since diagnosis etc. All data was collected by me and documented on paper. All data collection was done at the records department and in the pathology department. No patient identifier was recorded hence strict confidentiality was maintained.

Data analysis

The data gathered via questionnaires were then computed in Microsoft excel. Frequency tables, bar graphs, histograms and pie charts were constructed to show a representation of the data obtained. The data was also analyzed in Statistical Package for Social Science (SPSS) 64-bit edition to determine simple statistics such as mean survival times, survival charts were constructed using Kaplan Meier curve and log rank(mantel-cox) test was used to determine if there is significant relationship between data sets.

Potential benefits of this study

The data collected will give us an idea as to whether a nationwide screening program is needed to detect polyps and early cancer as is done in UK, USA, and other countries by identifying the stage at presentation of our colorectal cancer population. It will also help us to identify if patients are really benefiting from our MDT boards consultation. It might be able to show us if our management (surgical and medical) is comparable with what is accepted according to evidence-based medicine. Based on results specific interventions can be introduced to target risk factors, identify areas in our management that might need improvement, and to identify early colorectal cancer etc.

Results

After searching for patients with colorectal cancer, 118 charts were found with this diagnosis but after a careful review of each chart and a cross reference to all of the pathology reports for the study time period, only 32 charts were actually diagnosed with colorectal cancer. 2 of these charts were excluded due to lack of data for this study and 86 excluded due to inaccurate diagnosis. Which included, colonic polyps, hyperplastic adenomas, colonic dysplasia, gastric cancer etc (Figure 1).

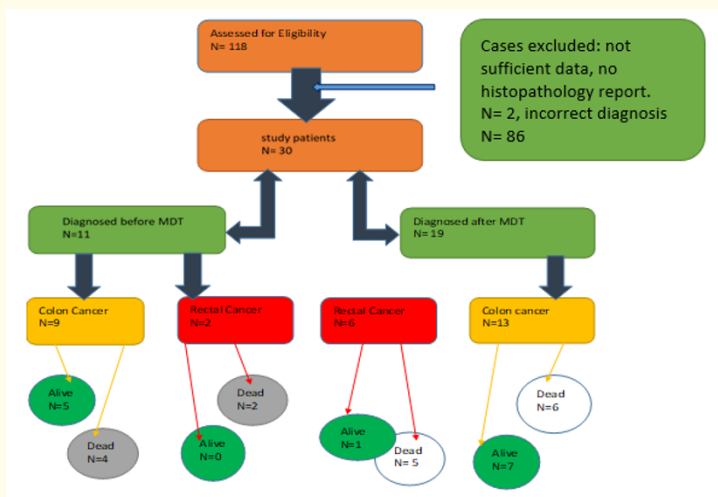


Figure 1: Number of cases in the study and their outcomes.

The majority of patients were diagnosed at the Dr. Orlando smith hospital, but some patients were referred from private institutions for further investigations and also as emergencies requiring acute surgical care. The mean age at diagnosis was 70.2 years (SD = 10.32), the youngest patient was 55 years and the oldest 94years old (Figure 2).

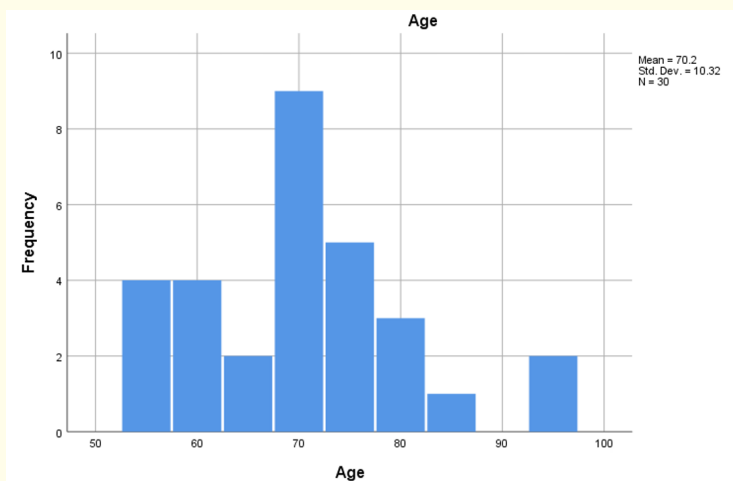


Figure 2: Ages of patient diagnosed with Colorectal cancer.

The mean ages of females at diagnosis with colon and rectal cancer were 66 years and 72 years respectively. For males it was 72 years for colon cancer and 74 years for rectal cancer. There was male predominance with 60% of patients being male and 40% female (Figure 3).

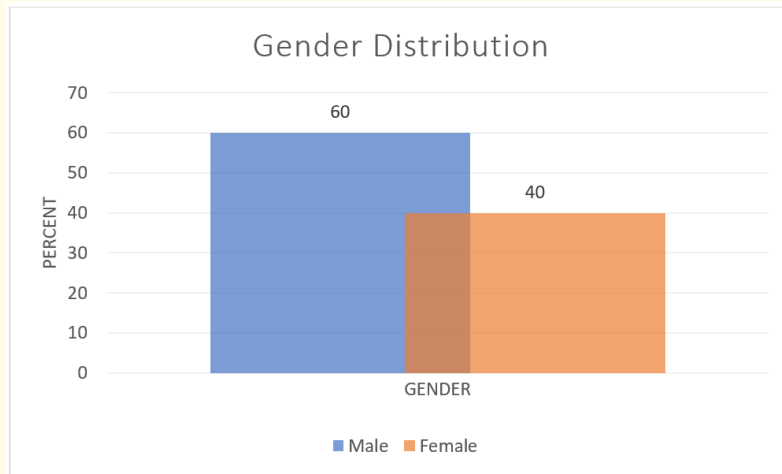


Figure 3: Gender distribution of the patients.

Left sided lesions were most common representing 43% of colon cancer (Figure 4).

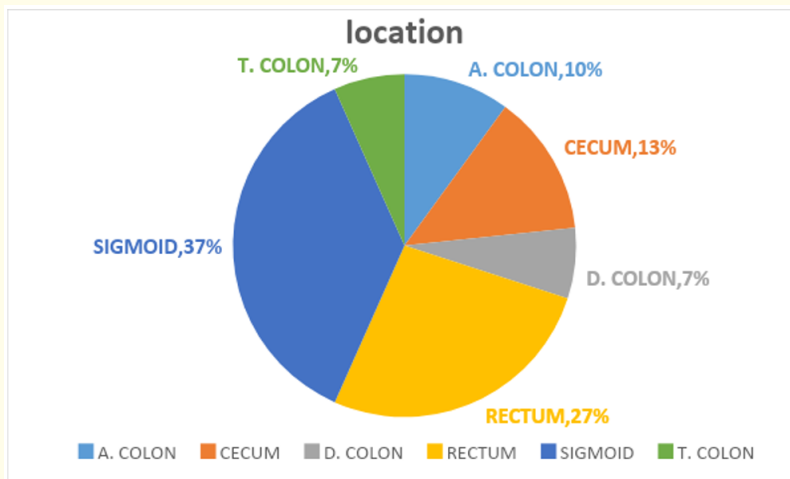


Figure 4: Pie chart showing the location of colorectal cancers.

with sigmoid colon being most frequent cancer 37%, followed by rectal cancer accounting for 27% of the cases and right sided cancer 30% of the cases. Mortality from right and left sided colon cancer was almost the same 44% and 46% respectively. However, 88% of patients with rectal cancer died, 75% presented at stage 4 and 25% at stage 3.

The most frequent presentation was LGIB/Per rectal bleeding (37%) (Figure 5).

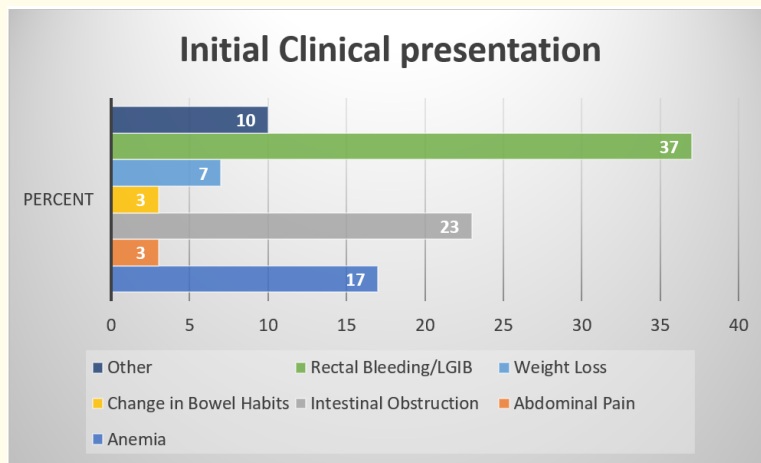


Figure 5: Initial clinical presentation of patients with colorectal cancer.

followed by intestinal obstruction (23%). The majority of patients presented at stage 4 (43%), followed by stage 1 (37%), stage 3 (17%) and stage 2(3%) (Figure 6).

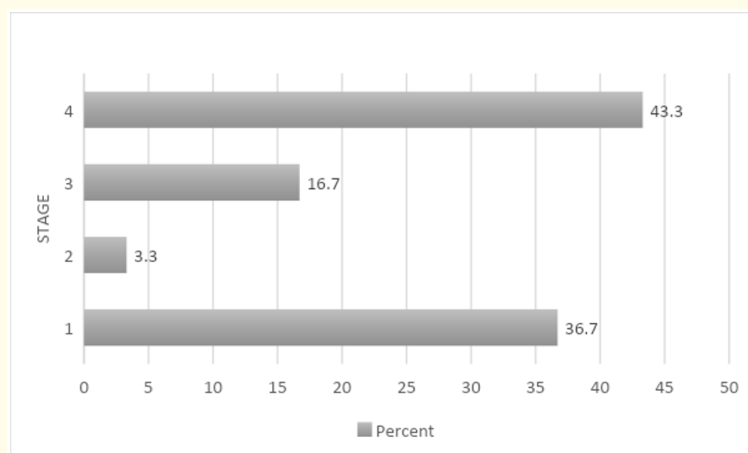


Figure 6: The percentage of patients represented by the different stages of colon cancer.

About 90% of the patients had not done any screening before diagnosis (FOB +/- colonoscopy) (Figure 7).

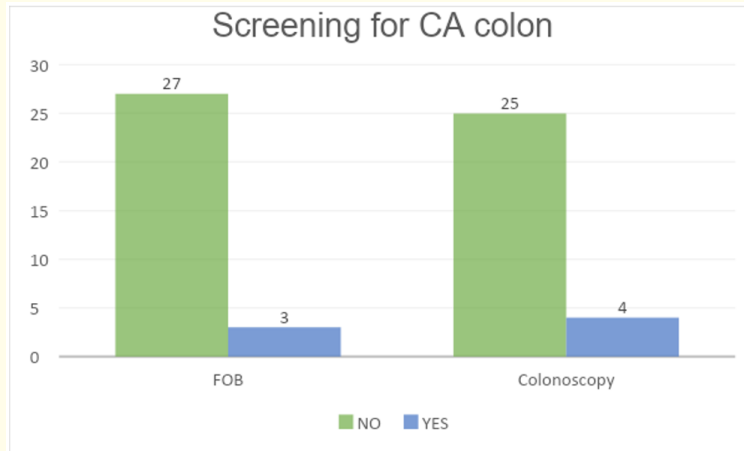


Figure 7: Screening for colorectal cancer in study group.

The overall mean survival time was 16.7 months (Figure 8).

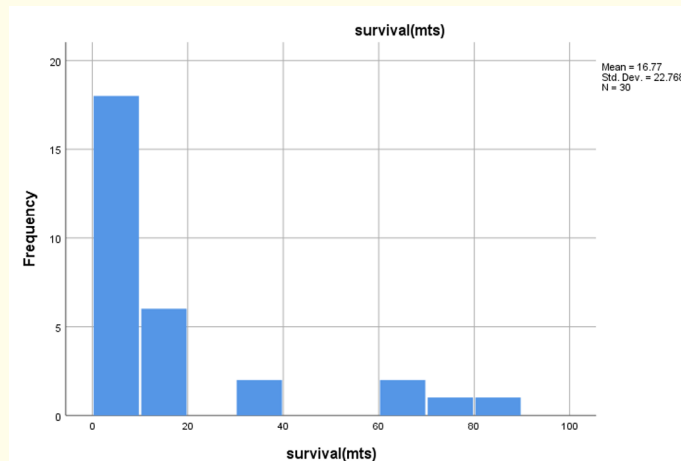


Figure 8: Survival time in months of patients with colorectal cancer.

Less than 1 month being the least time and 82 months being most time since diagnosis. The mean survival of stage 1 patients was 25 months, 72 months for stage 2, 13 months for stage 3 and 7 months for stage 4 (Figure 9).

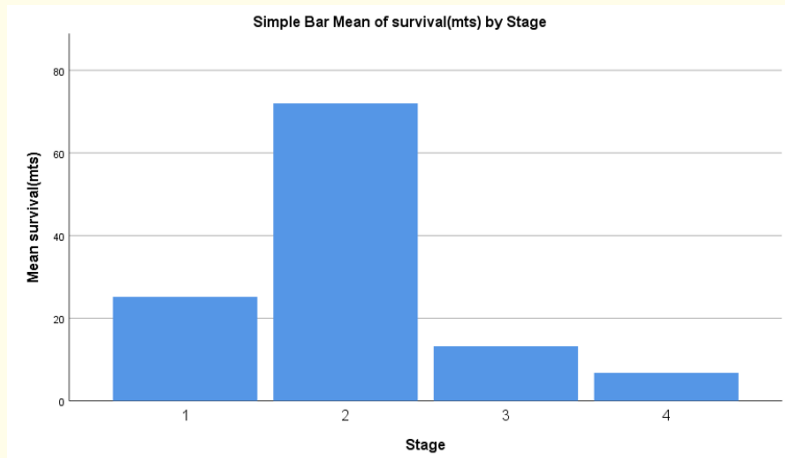


Figure 9: The mean survival time of the different stages of colorectal cancer.

Comparing stages and survival time there was statistical significance in Kaplan survival curve (log rank= 0.019) (Figure 10 and Table A).

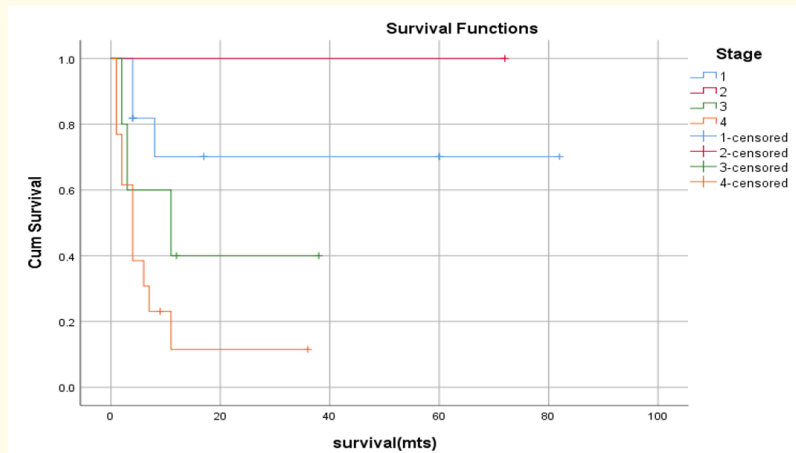


Figure 10: Kaplan Meier survival curve for different stages of colon cancer.

Overall Comparisons			
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	9.937	3	.019
<i>Test of equality of survival distributions for the different levels of Stage.</i>			

Table A

Approximately 63% of the cases were discussed at MDT boards, only 26% of patients did not adhere to MDT recommendations due to various factors, such as availability of finance to do radiotherapy abroad, family not in agreement etc. However, there was no significant relationship between disease survival and being discussed at MDT (log Rank = 0.600) (Figure 11 and Table B).

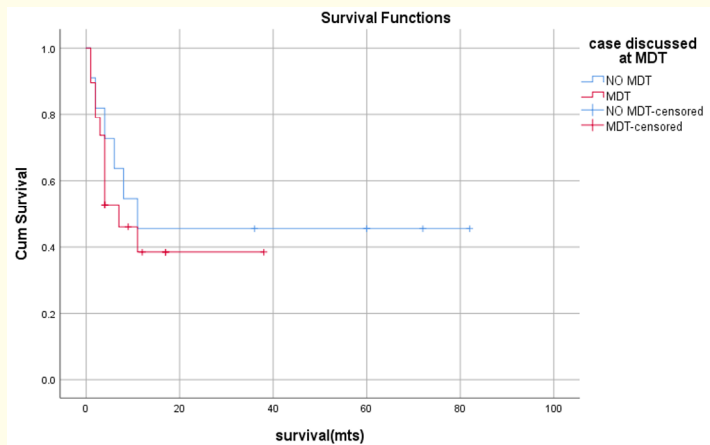


Figure 11: Kaplan Meier survival curve for cases discussed and not discussed at MDT.

Overall Comparisons			
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.275	1	.600
Test of equality of survival distributions for the different levels of case discussed at MDT.			

Table B

The mean survival time for women was 54 months and for men 21 months. Therefore, there was a statistical difference in survival times according to sex represented by log rank (p= 0.05) (Figure 12 and Table C).

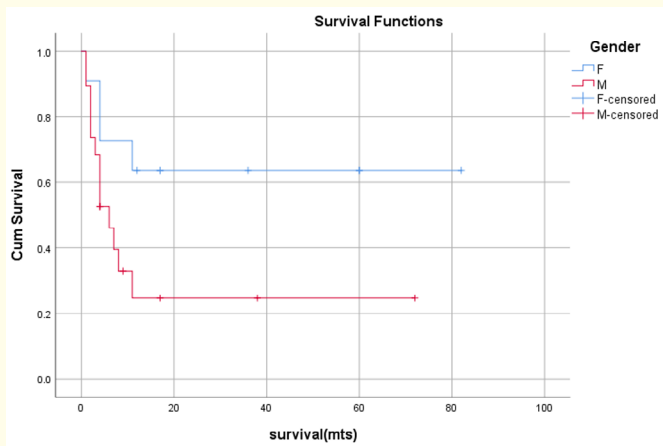


Figure 12: (Kaplan Meier survival curve for different gender with colon cancer).

Overall Comparisons			
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	3.790	1	.052
Test of equality of survival distributions for the different levels of Gender.			

Table C

At the end of this study 57% of the patients who were diagnosed with colorectal cancer died (Table 1).

Status of Patient	Frequency	Percent
alive	13	43.3
dead	17	56.7
Total	30	100

Table 1: Percentage of patients that are alive and those who died form study group.

70% of the patients had some form of surgical intervention and of those that had surgery 24% had some surgical complication post operatively (Table 2) the most frequent complication being anastomotic leak (14%).

Patie+A1:Age	Stage	NCEPOD	Type of Surgery	Time to Surgery (days)	Tumor size(cm)	Lymph Node yield	Post operative complications	Status	Location of Tumor
M	74	2	urgent SC	1	6	0	no	alive	sigmoid
F	56	1	elective SC	60	5	6	no	alive	sigmoid
F	58	1	urgent SC	1	5	8	no	alive	sigmoid
M	74	4	elective APR	42	3	0	no	dead	rectum
M	72	3	urgent LHC	3	8	10	no	dead	transverse colon
F	73	1	elective SC	72	2	0	yes	dead	sigmoid
M	57	4	urgent C	1	nil	nil	no	dead	sigmoid
F	58	1	elective TC	na	na	na	no	alive	transverse colon
M	82	1	urgent APR	1	6	0	no	alive	cecum
M	68	4	elective C	24	nil	nil	no	dead	sigmoid
F	68	1	elective RHC	20	6	11	no	alive	cecum
M	72	1	elective RHC	33	4	5	no	alive	cecum
F	71	3	elective SC	184	6	8	no	alive	sigmoid
M	77	3	elective LAP	231	7	nil	yes	alive	rectum
F	55	1	elective RHC	na	na	na	no	alive	ascending colon
M	71	4	urgent C	1	nil	nil	no	alive	descending colon
M	55	4	elective LHC	19	nil	nil	no	dead	sigmoid
M	73	4	elective LAP	31	nil	nil	no	dead	rectum
M	80	1	urgent SC	2	7	10	yes	alive	sigmoid
F	70	1	elective RHC	132	4	5	yes	dead	ascending colon
M	66	3	elective APR	22	5	4	yes	dead	rectum
APR- abdominoperineal resection				TC- transverse colectomy					
SC- sigmoid colectomy				LAP- low anterior resection					
RHC- right hemicolectomy				na- not available					
LHC- left hemicolectomy									
C- colostomy									
AP- appendectomy									

Table 2: Types of surgery performed for patients with colorectal cancer, time to surgery, tumor location etc.

The mean time to surgery from diagnosis to the surgical table for elective cases was 58days. This was the same pre-MDT and Post MDT. Emergencies accounted for 57% of the cases pre-MDT and post MDT 25% of the cases were emergencies. The average waiting time for emergencies was usually 1 day.

All the patients were diagnosed with adenocarcinoma of the rectum or colon. The mean lymph nodes yield at surgery was 5 and the average size of tumor removed was 5.3 cm. Of the 12 patients with stage 4 cancer 66% had metastasis to the liver.

50% of the CRC patients were hypertensive and 33% were diabetic, 30% of these patients were both hypertensive and diabetic.

The death rate was almost the same pre and post MDT, 54% and 57% respectfully. The one-year survival pre-MDT was 63%, higher than after the 1st year the MDT was implemented, 47% (Table 3). At 3yrs the rate was a little closer but pre-MDT patients still had a better survival rate.

Year of Diagnosis	Patients	Year 1	Year 2	Year 3	Survival
2013	2	2	2	2	p1 = 0.63
2014	2	2	1	1	p2 = 0.45
2015	3	2	1	1	p3 = 0.45
2016	4	1	1	1	
MDT					
2017	6	2	1	1	p1 = 0.47
2018	6	4	4		p2 = 0.39
2019	7	3			p3 = 0.39
total	30	16	10	6	

Table 3: Life table showing 1 to 3 year survival pre and post MD.

Discussion

In the BVI population colorectal cancer was mostly diagnosed in persons 55 years and above, there was one case of a male patient with crohn’s 34 years with colon cancer, but patient chart lacked enough information to be included in the study. The mean age of female patients with colorectal cancer (66 years) were younger than the males (72 years) which is the reverse to what is seen in the United States. (males 68, females 72) [47]. The increase in the under 50years with colon cancer was not seen in the BVI as was seen in the US and other western registries [19].

Globally there is equal distribution of colorectal cancer between males and females (1:1) however in our study population males were more likely to have colorectal cancer (3:2 distribution).

Left sided colorectal cancer was the most frequent cancer representing 70% of colorectal cancers with sigmoid colon responsible for the majority of cases (37%). No right sided shift was seen as is the current trend. The most frequent presentations as expected were LGIB and obstructive symptoms since there was a predominance of left sided lesions. In right sided lesions patients usually present later with anemia and weight loss. Right sided lesions carry a worst prognosis because they are detected late and are considered genetically different from left sided colorectal cancer [12,13,48].

Most of the patients presented to the hospital at a stage where the disease was curable (stage 1 - 3, 57%) there was also an equal amount of advance disease, stage 4(43%), which by itself is a poor prognostic factor. Curative surgery was the dominant strategy for 50%

of the patients, which involved open colonic resection. The complication rate post-operatively for colorectal cancer was 24% which is lower than what is seen in previous studies. Some studies report values of 30% and 28% [59,60]. However, our anastomotic leak rate was quite high at 14%, generally in most studies it varies from 3% to 4% but it can reach to 10% [56-59]. Anastomotic leak increases mortality and morbidity and leads to reoperation in the majority of cases. Risk factors include a pre-operative albumin level lower than 3.5g/dl, operative time of 200 minutes or longer, intraoperative blood loss of 200 ml or more, intraoperative transfusion and a histological specimen margin involvement in disease process in patients with inflammatory bowel disease [56]. Proximal diversion should be considered if all 3 intraoperative risk factors are present [56]. Colonic diversion should also be considered if bowel cleanliness is poor [57]. Most of these factors were not collected in this research paper but may be this can shine a light into why our anastomotic leak rate was high and can be evaluated in future studies.

Surgical waiting time from diagnosis to operating theater was prolonged for elective cases, 58 days both pre-MDT and post-MDT. However, the majority of patients waited less than 42 days but as a result of a couple of outlying data the mean waiting times were skewed upwards. The waiting times post MDT was significantly lower compared to pre-MDT. Cancer care Ontario recommends surgery within 42 days of diagnosis [21]. Several studies from Canada and Europe had an average waiting time to surgery around 32 days and they range from 0 days to 182 days but they all concluded that delay in time to surgery is not associated with poorer cancer specific and overall survival in patients with primary CRC who underwent curative surgical resection [20-24]. The waiting time for emergencies was usually 24 hrs.

After surgical treatment, patients were then referred for adjuvant chemotherapy/radiotherapy to an external clinical oncologist or sent overseas, since our hospital does not offer these services post resection. Data on these patients compliance, complications and follow up during chemotherapy were not available for most patients. Some patients defaulted on treatment (radiotherapy/ chemotherapy) due to family beliefs and others due to the unavailability of finance. Adjuvant chemotherapy plays an integral role in the treatment of micro metastasis especially in stage 3 disease after surgical resection and if not completed leads to progression of disease and decrease in overall survival of the patient.

The average tumor size removed was 5.3cm and the mean lymph nodes yielded was 5. Tumor size is an independent risk factor for cancer survival and the larger the tumor, there is increased risk of spread to lymph nodes and the worse the prognosis of the patient [49-52]. A lymph node yield of ≥ 12 nodes improves disease survival; hence patients were at a great disadvantage since on average only 5 nodes were removed at surgical resection. A greater effort by the surgeons is recommended to comply with what is done internationally to improve patient outcomes.

The overall survival of our cancer patients was 16.7 months, for stage 1-3 disease it was just about 2 yrs (24.4 mts) and stage 4 disease just 7 months. The 1 year survival before MDT was 63% and after MDT it dropped to 47%, this may be due to the increased amount of stage 4 patients that were diagnosed after MDT implementation. At 2 years pre and post MDT the survival rates were closer 45% and 39% respectively, but still surprising since MDT implementation was supposed to improve patient outcomes. In comparison to 1st world the UK and Wales have a 75% 1-year survival for colon cancer and 80% for rectal cancer, and at 5 years 60% of patients are still alive [54]. Studies done in other Caribbean islands with a more comparable population at one-year OS (overall survival) in Martinique was 74.6% and at 5 yrs it was 43.8% [55]. In Jamaica over a similar time period their 5 year survival was 33% [53].

Some of the factors which may be responsible for this unsatisfactory survival rate includes the stage at presentation of these patients which had statistical significance to the overall survival time ($p = 0.019$). There was also statistical significance between gender and overall survival as the average woman survived 4.5 years while the average male only survived 1.8 years ($p = 0.05$) and the majority 60%, of patients were males. Screening for colorectal cancer is another vital factor which is done by all 1st world countries and some 3rd world countries. 90% of our patients had no form of screening done prior to diagnosis. If a national program should be implemented, it will ben-

efit our population a great deal. It however should target patients between 55 to 75 years, since this range represents 77% of our cases and the remaining 23% are more advanced in age but premalignant lesions can and should be detected if they were screened earlier. Since the malignant transformation of adenoma to adenocarcinoma takes about 10 to 15 years and in the case of hereditary colorectal cancer these patients should be screened at age 40 or 10 years younger than the age at diagnosis of the youngest affected relative [26].

Hypertension is the most common comorbidity in cancer patients, and it was present in half of the CRC patients in this study. Diabetes was present in one third of the patients. Both hypertension and diabetes are risk factors for CRC [61-65]. A study done by Ahmadi, A., *et al* in 2014 found that there was no significant difference between the survival time of CRC patients suffering from hypertension and diabetes. However, a study in 2018 by Klaudia, K., *et al* found that patients with early colorectal cancer with hypertension had a significant greater risk of recurrence and death after treatment [61]. Chemotherapy itself is cardiovascular risk factor and compounded with uncontrolled hypertension maybe responsible for the increased in death observed.

The main goal of this study to prove that there was some improvement after the implementation of the MDT in overall survival proved the hypothesis to be false since there was no statistical difference of survival outcomes between patients seen before and after MDT ($p = 0.6$). 54% of the cases diagnosed with CRC pre- MDT and 57% post-MDT died at the end of this study.

Despite patients being reviewed by an expert panel after diagnosis(MDT), which is an independent risk factor for overall survival, these patients already present at a disadvantage, little screening is done prior to diagnosis, they present when little can be done (stage 4), they present with comorbidity (HTN, DM etc.), they have large tumors > 4 cm, their lymph nodes yield at resection is less than 12 and they have to be referred for adjuvant chemotherapy if required.

Limitations of Study

There are private health care facilities to which cancer patients attend so this study was unable to capture all the patients with colon cancer in the BVI. Unfortunately, over the study period there was also no cancer registry from which this data could be extracted. As this is a retrospective study, there was no randomization of the data collected. Data for many patients were not available and the Sample population collected was small. There is risk of confounding bias and additionally, there may be confounding factors, that are not mentioned. The data recall was insufficient to determine disease free survival. Information about adjuvant chemotherapy to see if patient received treatment or if they defaulted, which could definitely affect the results were not obtained for some patients.

Recommendations

Hopefully from this study we can advocate for colorectal cancer screening from 55 to 75 years at the primary health care and in private practice level, especially in the male patients, the surgical team can implement standards to resect > 12 nodes at colonic resection and reduce anastomotic leak rate, additionally we can try to implement chemo/radio therapy services at our hospital, so that together with our MDT we can decrease overall survival of our CRC patients.

Since this is the first study of this nature on CRC to my knowledge future prospective studies should be done to capture to incidence and prevalence of CRC in the entire country and observe how things change with time and possibly larger dataset.

Conclusions

Our MDT board has done a tremendous job in guiding the management of our cancer patients in the BVI since late 2016, however the evidence does not support an improvement in patient overall survival in CRC after its implementation. The typical patient is usually male in their 70's, not screened prior to presentation. Presenting with LGIB or intestinal obstruction, at stage 4 (43%) or stage 1 (37%). 70%

cases are left sided lesions. 50% of patients usually receive surgical treatment, with a 24% post-operative complication rate and an above average anastomotic leak rate (14%).

The results of this study, although the numbers are small, can guide us to improve specific areas in our CRC care and therefore in the long run provide a more targeted approach since each region's demographics may be different, so we need to adapt strategies that will best suit our population.

Acknowledgements

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