

Assessment Of Body Mass Index As Prognostic Parameter In Management Of Metastatic Colorectal Cancer

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Abstract

Background: BMI decreases predict poor prognoses for patients with advanced CRC, and normal BMI was a predictive factor for high survival rate. Thus, BMI appears to be an independent predictive factor of CRC survival rates. **Objectives:** To assess the prognostic value of BMI and outcome in both groups of patients: normal & abnormal (overweight and obese). **Methods:** This study was done in medical oncology departments in Zagazig University and Maadi Military Hospital including all metastatic colorectal cancer patients in the duration January 2016 till January 2018 with total number of 186 patients. All patient were evaluated regarding epidemiological data and response to treatment and survival analysis. **Results:** Median progression-free survival (PFS) of the whole studied sample (N=186 patients) was 9 months with higher PFS in patients receiving Anti-EGFR and patients with normal BMI. Obesity is also associated with poorer prognosis and outcomes with normal median overall survival in normal and abnormal (over weight and obese) (26 vs. 21 months) but it did not reach the significant value, and also regarding PFS was (10 vs. 9 months) respectively with no significant difference but denoting better numerical prognosis with normal BMI patients. There were others factors studied their relation to OS revealing significant correlation as receiving previous adjuvant treatment significantly increase overall survival (P=0.001), resection of primary tumor (P=0.001), site of metastasis with lymph nodes metastasis showing best overall survival up to 39 months (P=0.02), time of metastasis as metachronous metastasis showed higher overall survival up to 39 months (P=0.001), and K-RAS status as wild profile showed better survival (P=0.015). **Conclusions:** patients with normal BMI achieved better results than those with abnormal BMI.

Keywords: Body Mass Index, Metastatic Colorectal Cancer

INTRODUCTION

Annually, approximately 147,950 new cases of large bowel cancer are diagnosed, 104,610 of which are colon cancer, and the remainder are rectal. Annually, approximately 53,200 Americans die of CRC, accounting for approximately 8 percent of all cancer deaths (1).

Colorectal cancer is the 7th commonest cancer in Egypt, representing 3.47% of male cancers and 3% of female cancers. The estimated number of colon cancer patients (excluding rectal cancer) in 2015 was slightly more than three thousand (2).

Some registries report a rising incidence of CRC even among young adults 20 to 39 years of age, although the absolute incidence in this age group remains far lower than for adults aged 50 or over (3,4).

These geographic differences appear to be attributable to differences in dietary and environmental exposures that are imposed upon a background of genetically determined susceptibility (5).

Low socioeconomic status (SES) is also associated with an increased risk for the development of colorectal cancer; one study estimated the CRC risk to be approximately 30 percent increase in the lowest as compared with the highest SES quintile (6).

Obesity which is characterized by an excess of body fat is an established risk factor for colorectal carcinogenesis (8).

A recent linear dose-response meta-analysis of four prospective studies showed that each 5 kg increase in adult weight gain was associated with an approximately 6% increased risk of colon cancer (RR = 1.06, 95% CI = 1.03–1.10) (9).

A study by Campbell et al found that prediagnosis BMI is an important predictor of survival among patients with nonmetastatic colorectal cancer (10).

BMI decreases predict poor prognoses for patients with advanced CRC, and elevated BMI was a predictive factor for high survival rate. Thus, BMI appears to be an independent predictive factor of CRC survival rates (11)

Subjects and Methods:

This is a retrospective study that assessed impact of BMI on mCRC prognosis. This study was done in Medical Oncology departments in Zagazig university and Maadi military hospital including metastatic colorectal cancer patients from January 2016 till January 2018 with total number of 186 patients.

Primary end point: - progression free survival.

Secondary end point: - overall survival.

All patient's characteristics correlated to BMI to assess its prognostic impact on patients outcome.

BMI classification according to WHO.

| BMI | Nutritional status |
|------------|--------------------|
| Below 18.5 | Underweight |
| 18.5–24.9 | Normal weight |
| 25.0–29.9 | Pre-obesity |
| 30.0–34.9 | Obesity class I |
| 35.0–39.9 | Obesity class II |
| Above 40 | Obesity class III |

We divided patients into 2 groups in our study regarding BMI:

Normal group: 18.5-24.9.

Abnormal group: ≥ 25

Inclusion criteria:-

- 1) Age more than 18 years old
- 2) Pathologically proved colorectal cancer.
- 3) Metastatic disease.
- 4) Performance status:0-2.
- 5) Available complete data

Exclusion criteria: -

- 1) Other malignancies.
- 2) Performance status: > 2 .

All patients were evaluated for: -

- 1) History.
- 2) Physical Examination.
- 3) Routine Laboratory Workup: CBC, kidney function tests, liver function test, CEA.
- 4) Radiological Workup: CT Chest, CT abdomen and pelvis.
- 5) Clinical and demographic data: - Age, gender, residence, body mass index, performance status, site of primary tumor, previous adjuvant treatment, Resectibility of primary tumor, site of metastasis, type of metastasis (synchronous or metachronous), KRAS status, BRAF status when available, receiving anti-EGFR and response to treatment, progression free survival and overall survival.

The systemic therapy used was either FOLFIRI or FOLFOX-4 with or without anti-EGFR as follow:

FOLFIRI plus (anti-EGFR):

panitumumab dose is 6 mg /KG IV over 2 hours plus irinotecan 180 mg/m² IV over 30-90 min on day 1 plus leucovorin 400 mg/m² IV infusion to match duration of irinotecan infusion on day 1 plus 5-FU 400 mg/m² IV bolus on day 1, then 1200 mg/m²/day for 2-d (total 2400 mg/m² over 46-48 h) continuous infusion; repeat every 2 wk.

In case of Cetuximab 500mg/ m² IV over 2 hours and received every 2 weeks.

Patients received FOLFIRI were 62 patients, 10 patients of them received anti-EGFR (Cetuximab)

FOLFOX-4 plus (anti-EGFR):

Day 1: Oxaliplatin 85 mg/m² IV and leucovorin 200 mg/m² IV over 120 minutes followed by 5-FU 400 mg/m² IV bolus given over 2–4 minutes, followed by 5-FU 600 mg/m² IV over 22-hour continuous infusion.

Day 2: Leucovorin 200 mg/m² IV infusion over 120 minutes, followed by 5-FU 400 mg/m² IV bolus given over 2–4 minutes, followed by 5-FU 600 mg/m² IV infusion over 22-hour continuous infusion.

Cetuximab 500mg/ m² IV over 2 hours or panitumumab dose is 6 mg /KG and administered like that of cetuximab and received every 2 weeks.

Patients received FOLFOX-4 were 124 patients out of which 37 patients received anti-EGFR.

Results

Our study included 186 patients.

The majority of patients were with age mean 59 years, with higher incidence in males than females 109/186 (58.6%) vs. 77/186 (41.4%) respectively with higher number of patients from urban residence 123/186 (66.1%) vs. 63/186 (33.9%) from rural residence and BMI of patients divided into normal 67/186 (36%) patients, abnormal 119/186 (64%) patients.

153/186 patients (82.3%) were with performance status 1 vs. 33/186 patients (17.7%) with performance status 2.

Median CEA 6.25 ng/mL range (0-5659) at time of diagnosis.

Majority of cases with left colon cancer 147/186 (79%) vs. 39/186 (21%) case of right colon cancer, 60/186 patients (32.3%) received adjuvant treatment before being metastatic vs. 126/186 (67.7%) who did not receive adjuvant chemotherapy as they were metastatic from the start.

117/186 (62.9%) patients had resected 1ry tumor vs. 69/186 (37.1%) who did not undergo resection of 1ry tumor.

Site of metastasis vary widely between different cases as follow:-

Liver metastasis were reported in 52/186 (28.0%) of patients, while lung metastasis were reported in 7/186 (3.8%) of patients, LNS metastasis were reported in 22/186 (11.8%) of patients, 11/186 (5.9%) patients showed peritoneal deposits and adnexal lesions, with 91/186 patients (48.9%) show multiple metastasis and 3/186 patients (1.6%) showing other metastasis either bone or brain metastasis.

Synchronous metastasis were discovered in 124/186 (66.7%) while Metachronous metastasis occur in 62/186 (33.3%) of patients.

K-RAS status was done to 117 patients. Out of 117 patients 73 were wild type and 44 were mutant.

While BRAF status among patients was as follow: majority of the patients were not reported 171/186 (91.9%) while 14/186 (7.5%) were wild type and only 1/186 patient (0.5%) was mutant type.

Among whole patients 47/186 (25.3%) patients received 5FU based chemotherapy plus anti-EGFR vs. 139/186 (74.7%) patients received 5FU based chemotherapy alone. Various responses to treatment occur about 97/186 (52.2%) of patients showed progressive course while 86 /186 (46.2%) of patients showed stationary course and 3 /186patients (1.6%) showed partial response.

Chemotherapy received was either FOLFOX-4 received by 124 patients or FOLFIRI received by 62 patients.

Table (1):- Progression free survival and overall survival of the patients.

| Survival data | | No. = 186 |
|---|-------------|--------------|
| PFS (mos) date of Dis. progression After 1st line | Median(IQR) | 9 (6 – 12) |
| | Range | 2 – 30 |
| OS (mos) since diagnosis till death or last visit | Median(IQR) | 18 (11 - 29) |
| | Range | 2 – 51 |

As shown in table (1):-

Median PFS among whole study group was 9 months ranged from 2-30 months, while median overall survival was 18 months ranged from 2-51 months.

Table (2):- Survival status.

| Survival status | No. | % |
|-----------------|-----|--------|
| Alive | 66 | 35.5% |
| Dead | 120 | 64.5% |
| Total | 186 | 100.0% |

As shown in table (2):-

Among all included patients 66/186 patients (35.5%) were alive and 120/186 (64.5%) patients died.

Table (3):- Correlation between BMI and demographic data and patients characteristics.

| Variable | | BMI category | | P-value |
|-------------------|--------------|---------------|----------------|---------|
| | | Normal | Abnormal | |
| | | No. = 67 | No. = 119 | |
| Age | Mean ± SD | 55.64 ± 14.77 | 60.42 ± 11.58 | 0.016 |
| | Range | 22 – 75 | 27 – 81 | |
| Sex | Male | 49 (73.1%) | 60 (50.4%) | 0.003 |
| | Female | 18 (26.9%) | 59 (49.6%) | |
| Ecgog | 1 | 60 (89.6%) | 93 (78.2%) | 0.051 |
| | 2 | 7 (10.4%) | 26 (21.8%) | |
| Residence | Urban | 43 (64.2%) | 80 (67.2%) | 0.673 |
| | Rural | 24 (35.8%) | 39 (32.8%) | |
| CEA initial | Median (IQR) | 7 (3 – 43) | 6 (2.9 – 44.9) | 0.805 |
| | Range | 0.27 – 5659 | 0.1 – 4164 | |
| Site of 1ry tumor | Left colon | 52 (77.6%) | 95 (79.8%) | 0.721 |

| | | | | |
|---|--------------------------------|--------------|--------------|-------|
| | Right colon | 15 (22.4%) | 24 (20.2%) | |
| Previous adjuvant treatment | Yes | 18 (26.9%) | 42 (35.3%) | 0.238 |
| | No | 49 (73.1%) | 77 (64.7%) | |
| Resected Iry tumor | Yes | 41 (61.2%) | 76 (63.9%) | 0.717 |
| | No | 26 (38.8%) | 43 (36.1%) | |
| Site of metastasis | Liver | 20 (29.9%) | 32 (26.9%) | 0.041 |
| | Lung | 1 (1.5%) | 6 (5.0%) | |
| | LNS | 14 (20.9%) | 8 (6.7%) | |
| | peritoneal deposits and adnexa | 3 (4.5%) | 8 (6.7%) | |
| | others(brain or bone) | 0 (0.0%) | 3 (2.5%) | |
| | Multiple site metastasis | 29 (43.3%) | 62 (52.1%) | |
| Type of metastasis | Synchronous | 50 (74.6%) | 74 (62.2%) | 0.084 |
| | Metachronous | 17 (25.4%) | 45 (37.8%) | |
| K-RAS | Wild | 28 (41.8%) | 45 (37.8%) | 0.665 |
| | Mutant | 17 (25.4%) | 27 (22.7%) | |
| | Not reported | 22 (32.8%) | 47 (39.5%) | |
| BRAF status | Wild | 6 (9.0%) | 8 (6.7%) | 0.652 |
| | Mutant | 0 (0.0%) | 1 (0.8%) | |
| | Not reported | 61 (91.0%) | 110 (92.4%) | |
| Received Anti EGFR+5FU based chemotherapy | Received | 17 (25.4%) | 30 (25.2%) | 0.980 |
| | Not received | 50 (74.6%) | 89 (74.8%) | |
| Response to treatment | Progressive course | 27 (40.3%) | 70 (58.8%) | 0.048 |
| | Stationary course | 39 (58.2%) | 47 (39.5%) | |
| | Partial response | 1 (1.5%) | 2 (1.7%) | |
| PFS (mos) date of Dis.prog. After 1st line | Median (IQR) | 10 (7 – 12) | 9 (6 – 12) | 0.402 |
| | Range | 2 – 30 | 2 – 24 | |
| OS (mos) since diagnosis till death or last visit | Median (IQR) | 19 (10 – 31) | 17 (11 – 28) | 0.712 |
| | Range | 2 – 46 | 3 – 51 | |
| Survival status | Alive | 25 (37.3%) | 41 (34.5%) | 0.696 |
| | Dead | 42 (62.7%) | 78 (65.5%) | |

Abnormal group including (overweight and obese)

Normal BMI was found in younger age group with median age 55.6 years and range (22-75) years while abnormal BMI was noticed in older age group with median 60.4 years with range (27–81) years with significant relation (P=0.016).

In correlation of BMI and sex there was highly significant relation as in normal BMI group there was 49/67 (73.1%) males vs. 60/119 (50.4%) in abnormal group, while females in normal group were 18/67 (26.9%) vs. 59/119 (49.6%) in abnormal group denoting increase number of both males and females in abnormal BMI group but with marked difference in female gender more than that of male (P=0.003).

Relation between BMI and performance status was found insignificant, in normal group ECOG 1 were 60/67 (89.6%) patients vs. 93/119 (78.2%) in abnormal group, while performance status 2 in normal group was 7/67 (10.4%) vs. 26/119 (21.8%) (P= 0.051).

Regarding residence, in normal group 43/67 (64.2%) patients were living in urban areas vs. 80/119 (67.2%) in abnormal group denoting higher BMI of patients in urban areas. While in normal group 24/67 patients (35.8%) lived in rural areas vs. 39/119 (32.8%) in abnormal group with no significant difference (P=0.673).

In correlation to initial CEA, in normal BMI group median CEA was 7 ng/mL with range (0.27 – 5659) ng/mL while in abnormal group median CEA was 6 ng/mL with range (0.1 – 4164). With no significant difference (P=0.805).

Relation between site of Iry tumor and BMI, in normal BMI group 52/67 (77.6%) patients was with left colon tumors vs. 95/119 (79.8%) patients in abnormal group denoting higher incidence of abnormal BMI in left colon tumors, while patients with right sided tumors in normal group 15/67 patients (22.4%) vs. 24/119 patients (20.2%) in abnormal group, with no significant value (P=0.721).

No significant relation between BMI and received adjuvant treatment (P=0.238), or resected Iry tumor (P=0.717).

In correlation of BMI and site of metastasis, multiple site metastasis were more in abnormal group 62/119 patients (52.1%) vs. 29/67 patients (43.3%) in normal group BMI, while liver metastasis in normal group were 20/67 patients (29.9%) higher than that in abnormal group 32/119 patients (26.9%), also lymph nodes metastasis incidence in normal group of BMI were higher 14/67 patients (20.9%) vs. 8/119 patients (6.7%) patients in abnormal group, lung metastasis were more in abnormal BMI group 6/119 (5%) patients vs. 1/67(1.5%) patient in normal group, peritoneal deposits and adnexa were higher in abnormal BMI 8/119 patients (6.7%) vs. 3/67 patients (4.5%) patients in normal group. Other metastasis (brain and bone) were found in abnormal group 3/119 patients (2.5%) vs. no patients in normal group with significant differences. (P=0.041)

There was no significant correlation between BMI and metastasis being Synchronous or Metachronous as in normal BMI group

Synchronous metastasis occurred in 50/67 (74.6%) patients vs. 74/119 (62.2%) patient in abnormal group denoting higher incidence of Synchronous metastasis in normal BMI group. While in abnormal BMI group Metachronous metastasis occurred in 17/67 patients (25.4%) vs. 45 /119 patients (37.8%) of abnormal group, denoting higher incidence of Metachronous metastasis in abnormal BMI group with no significant difference (P=0.084).

In correlation of BMI and KRAS status, in normal BMI group wild type were 28/67 patients (41.8%) vs. 45/119 patients (37.8%) patients in abnormal BMI group denoting higher incidence of wild KRAS in normal BMI group.

Mutant KRAS profiles in normal group were 17/67 (25.4%) patients vs. 27/119 patients (22.7%) patients in abnormal group denoting higher incidence of mutant KRAS in normal BMI group. 22/67 patients (32.8%) were not reported in normal and 47/119 patients (39.5%) were not reported in abnormal group with insignificant difference (P=0.665).

Correlation between BRAF status and BMI revealed insignificant relation, in normal BMI group 6/67 (9%) were wild vs. 8/119 patients (6.7%) in abnormal group denoting higher incidence of wild type BRAF in normal BMI group, while in abnormal group of BMI 1/119 patient (0.8%) showed mutant BRAF while in normal group no patients showed mutant BRAF denoting higher incident of mutant BRAF in abnormal group, 61/67 patients (91.0%) in normal group vs. 110/119 patients (92.4%) in abnormal group were not reported. With insignificant value (P=0.652).

There is no significant relationship between BMI and receiving Anti EGFR plus 5FU based chemotherapy (P=0.980).

Correlation between BMI and response to treatment showed significant relationship, in normal BMI group 27/67 patients (40.3%) showed progressive response to treatment vs. 70/119 patients (58.8%) in abnormal group denoting poorer response with abnormal BMI group. While in normal group 39/67 patients (58.2%) showed stationary response vs. 47/119 patients (39.5%) in abnormal group denoting better response to treatment in normal BMI group, while partial response occurred in normal BMI group in 1/67 patients (1.5%) vs. 2/119 patients (1.7%) in abnormal group with significant difference (P=0.048).

Relation between BMI and progression free survival was insignificant showing in normal group BMI median PFS was 10 months with range (2-30) months vs. 9 months with range (2-24) months with no significant difference (P=0.402).

Correlation between BMI and overall survival revealed insignificant relation between them as in normal BMI group median overall survival was 19 months with range (2-46) months vs. 17 months with range (3-51) months with no significant difference (P=0.712).

Relation between BMI and survival status showed in normal BMI group 25/67 patients (37.3%) vs. 41/119 patients (34.5%) patients of abnormal group still alive. Also in normal BMI group 42/67 patients (62.7%) vs. 78/119 patients (65.5%) patients in abnormal group are dead denoting better survival status with normal BMI group but did not reach significant value (P=0.696).

Table (4): Overall survival among whole patient group

| OS (months) | | 95% Confidence Interval | | OS at (%) (months) | | | |
|-------------|-------|-------------------------|--------|--------------------|-------|-------|------|
| Median | SE | Lower | Upper | 12m | 24 m | 36 m | 48 m |
| 22.0 | 1.735 | 18.599 | 25.401 | 68.2% | 44.4% | 33.1% | 9.4% |

Median overall survival of all patients was 22 months

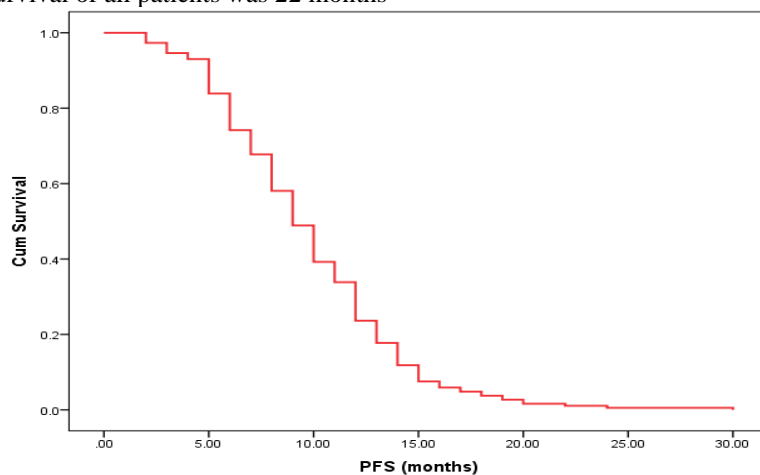


Figure (1):- Progression free survival among whole patient group.

Table (5):- Progression free survival among whole patient group.

| PFS (months) | | 95% Confidence Interval | | PFS at (%) | | |
|--------------|-------|-------------------------|-------|------------|-----------|-----------|
| Median | SE | Lower | Upper | 6 months | 12 months | 18 months |
| 9 | 0.390 | 8.236 | 9.764 | 74.2% | 23.7% | 3.8% |

Median progression free survival of all patients was 9 months

Table (6):- Relation of overall survival and all demographic data and patients characteristics.

| | | Total N | OS (months) | | 95% CI | | P-value |
|---|--------------------------------|---------|-------------|--------|--------|--------|---------|
| | | | Median | SE | Lower | Upper | |
| Age | ≤ 59 | 78 | 30 | 4.652 | 20.883 | 39.117 | 0.162 |
| | > 59 | 108 | 20 | 1.799 | 16.474 | 23.526 | |
| Sex | Male | 109 | 24 | 2.554 | 18.994 | 29.006 | 0.230 |
| | Female | 77 | 16 | 1.949 | 12.181 | 19.819 | |
| Ecog | 1 | 153 | 22 | 2.330 | 17.433 | 26.567 | 0.375 |
| | 2 | 33 | 21 | 5.299 | 10.614 | 31.386 | |
| BMI category | Normal | 67 | 26 | 4.969 | 16.261 | 35.739 | 0.811 |
| | Abnormal | 119 | 21 | 1.913 | 17.25 | 24.75 | |
| Residence | Urban | 123 | 23 | 2.324 | 18.444 | 27.556 | 0.904 |
| | Rural | 63 | 21 | 2.769 | 15.573 | 26.427 | |
| Site of 1ry tumor | Left colon | 147 | 23 | 2.855 | 17.403 | 28.597 | 0.241 |
| | Right colon | 39 | 18 | 2.665 | 12.777 | 23.223 | |
| Previous adjuvant treatment | Yes | 60 | 39 | 4.920 | 29.356 | 48.644 | <0.001 |
| | No | 126 | 15 | 1.721 | 11.627 | 18.373 | |
| Resected 1ry tumor | Yes | 117 | 30 | 3.466 | 23.206 | 36.794 | <0.001 |
| | No | 69 | 11 | 1.130 | 8.786 | 13.214 | |
| Site of metastasis | Liver | 52 | 24 | 3.150 | 17.825 | 30.175 | 0.021 |
| | Lung | 7 | 19 | 9.165 | 1.036 | 36.964 | |
| | LNS | 22 | 39 | 5.567 | 28.088 | 49.912 | |
| | peritoneal deposits and adnexa | 11 | 10 | 2.890 | 4.336 | 15.664 | |
| | others(brain or bone) | 3 | 23 | . | . | . | |
| Type of metastasis | Multiple site metastasis | 91 | 21 | 1.923 | 17.231 | 24.769 | <0.001 |
| | Synchronous | 124 | 15 | 1.582 | 11.900 | 18.100 | |
| K-RAS | Metachronous | 62 | 39 | 5.009 | 29.182 | 48.818 | 0.015 |
| | Wild | 73 | 39 | 9.588 | 20.207 | 57.793 | |
| Received Anti EGFR+5FU based chemotherapy | Mutant | 44 | 21 | 0.709 | 19.611 | 22.389 | 0.002 |
| | Received | 47 | 47 | 19.339 | 9.096 | 84.904 | |
| | Not received | 139 | 21 | 2.109 | 16.867 | 25.133 | |

In correlation of overall survival and patients age group above and below 59 years, it shows that median overall survival in age group ≤59 years old was 30 months vs. 20 months for those above 59 years with no significant relation (P=0.162).

In relation to sex median overall survival among males was 24 months vs. 16 months for females with no significant difference (P=0.230).

Correlation between performance status and overall survival did not reveal significant difference as median overall survival in performance status 1 was 22 months vs. 21 for patients with performance status 2 with insignificant difference (P=0.375).

BMI relation to overall survival shows median overall survival to normal BMI 26 months vs. 21 for those abnormal patients. With no significant difference (P=0.375).

In correlation of residence and overall survival, patients of urban areas had median overall survival 23 months vs. 21 for those of rural areas with insignificant value (P=0.904).

Site of primary tumor revealed insignificant relation to overall survival as patients of left colon cancer had median overall survival 23 months vs. those with right colon cancer had median overall survival 18 months with insignificant value (P=0.241).

In correlation of previous adjuvant treatment with overall survival, it reveals highly significant difference as patients who received previous treatment had median overall survival 39 months vs. 15 months for those who did not receive (P <0.001).

Also resection of primary tumor revealed high significance with overall survival as patients with resected primary tumor had median overall survival 30 months vs. 11 months for those who did not had tumor resection (p <0.001).

There is a significant relation between site of metastasis and overall survival as patients with lymph nodes metastasis had median overall survival 39 months while those who had liver metastasis had median overall survival 24 months. Other sites of metastasis

(brain and bone) showed median overall survival 23 months, patients with multiple sites metastasis showed median overall survival 21 months, lung metastasis patients had median overall survival 19 months and patients with peritoneal deposits and adnexa had median overall survival 10 months (P=0.021).

In correlation of overall survival and metastasis being Synchronous or Metachronous, patients with Synchronous metastasis showed median overall survival 15 months vs. 39 months for those with Metachronous metastasis showing significant difference in favor of Metachronous metastasis (p <0.001).

Correlation of KRAS status in patients who had tested it revealed significant relation with overall survival as patients with wild KRAS status had median overall survival 39 months vs. 21 months for those with mutant KRAS (P=0.015).

Among whole patients correlation of receiving anti-EGFR plus 5FU based chemotherapy with overall survival revealed highly significant relation as patients who received anti-EGFR plus 5FU based chemotherapy had median overall survival 47 months vs. 21 months for those who did not receive anti-EGFR plus 5FU based chemotherapy (P=0.002).

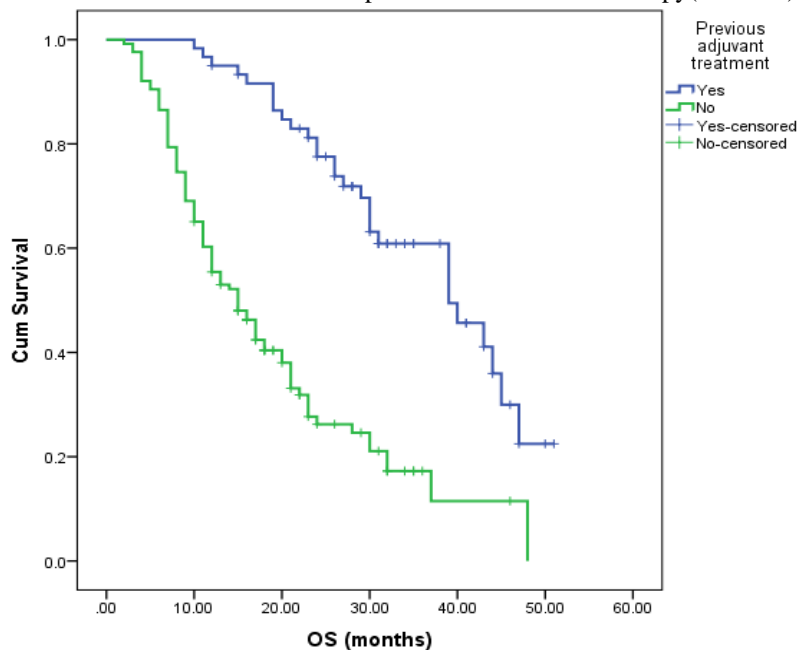


Figure (2):- Relation between receiving previous adjuvant treatment and OS (P<0.001).

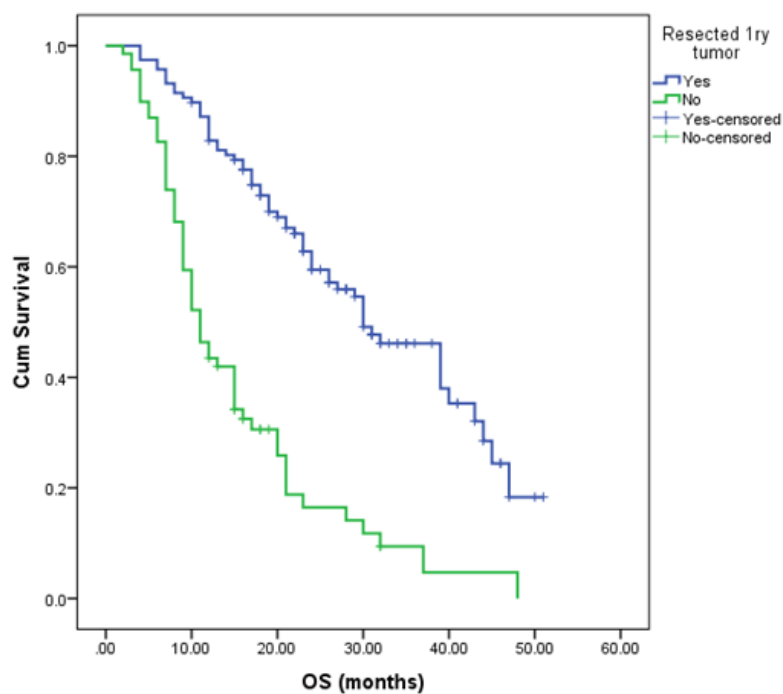


Figure (3):- Relation between resection of primary tumor and OS (P<0.001).

Table (7):- Relation between progression free survival and demographics and patient characteristics.

| Variable | | Total N | PFS (months) | | 95% CI | | P-value |
|--|--------------------------------|---------|--------------|-------|--------|--------|---------|
| | | | Median | SE | Lower | Upper | |
| Age | ≤ 59 | 78 | 8 | 0.552 | 6.918 | 9.082 | 0.868 |
| | > 59 | 108 | 10 | 0.427 | 9.163 | 10.837 | |
| Sex | Male | 109 | 10 | 0.466 | 9.087 | 10.913 | 0.804 |
| | Female | 77 | 9 | 0.457 | 8.104 | 9.896 | |
| ECOG | 1 | 153 | 9 | 0.412 | 8.192 | 9.808 | 0.848 |
| | 2 | 33 | 9 | 1.226 | 6.597 | 11.403 | |
| BMI category | Normal | 67 | 10 | 0.624 | 8.777 | 11.223 | 0.481 |
| | abnormal | 119 | 9 | 0.534 | 7.953 | 10.047 | |
| Residence | Urban | 123 | 9 | 0.427 | 8.164 | 9.836 | 0.716 |
| | Rural | 63 | 9 | 0.793 | 7.446 | 10.554 | |
| Site of Iry tumor | Left colon | 147 | 10 | 0.426 | 9.166 | 10.834 | 0.992 |
| | Right colon | 39 | 9 | 0.675 | 7.677 | 10.323 | |
| Previous adjuvant treatment | Yes | 60 | 10 | 0.350 | 9.313 | 10.687 | 0.024 |
| | No | 126 | 9 | 0.462 | 8.095 | 9.905 | |
| Resected Iry tumor | Yes | 117 | 10 | 0.569 | 8.885 | 11.115 | <0.001 |
| | No | 69 | 8 | 0.820 | 6.393 | 9.607 | |
| Site of metastasis | Liver | 52 | 10 | 0.509 | 9.002 | 10.998 | <0.001 |
| | Lung | 7 | 7 | 1.309 | 4.434 | 9.566 | |
| | LNS | 22 | 11 | 0.879 | 9.276 | 12.724 | |
| | peritoneal deposits and adnexa | 11 | 5 | 1.101 | 2.842 | 7.158 | |
| | others(brain or bone) | 3 | 11 | 1.633 | 7.799 | 14.201 | |
| Type of metastasis | Synchronous | 124 | 9 | 0.458 | 8.103 | 9.897 | 0.018 |
| | Metachronous | 62 | 10 | 0.655 | 8.717 | 11.283 | |
| K-RAS | Wild | 73 | 9 | 0.568 | 7.886 | 10.114 | 0.819 |
| | Mutant | 44 | 10 | 0.734 | 8.561 | 11.439 | |
| Received Anti EGFR+ 5FU based chemotherapy | Received | 47 | 9 | 0.623 | 7.779 | 10.221 | 0.838 |
| | Not received | 139 | 9 | 0.491 | 8.037 | 9.963 | |

As shown in table (7):-

In correlation of progression free survival and age there was no significant relation between them as patients group ≤ 59 had median progression free survival 8 months vs. 10 for those >59 years (P=0.868).

Sex and progression free survival did not show a significant relation as male patients had progression free survival 10 months vs. 9 for those of females (P=0.804).

In correlation with progression free survival, performance status did not show significant relation as both patient with performance status 1 and performance status 2 had PFS of 9 months (P=0.848).

BMI did not show significant correlation with progression free survival as normal BMI group had median progression free survival 10 months vs. 9 for those of abnormal BMI (P=0.481).

Patients of both urban and rural areas had median progression free survival 9 months with no significant difference (P=0.716).

Relation of primary tumor site and progression free survival is insignificant as patients with left colon cancer had median progression free survival 10 months vs. 9 months for those with right colon cancer (P=0.992).

In correlation to progression free survival receiving previous adjuvant treatment proved to improve progression free survival significantly as patients received previous adjuvant treatment had median progression free survival 10 months vs. 9 in those patients who did not receive (P=0.024).

Resection of primary tumor significantly increase PFS as patients with resected primary tumor had 10 months median progression free survival vs. 8 months for those who did not undergo resection (P<0.001).

Also site of metastasis showed to have highly significant relation with PFS as patients with lymph nodes metastasis had median progression free survival 11 months while those who had liver metastasis had median progression free survival 10 months, other sites of metastasis (brain and bone) showed median progression free survival 11 months, patients with multiple sites metastasis showed median progression free survival 9 months, lung metastasis patients had median progression free survival 7 months and patients with peritoneal deposits and adnexa had median progression free survival 5 months ($P=0.001$).

Correlation between PFS and metastasis being Synchronous or Metachronous showed significant relation as patients with Synchronous metastasis had median progression free survival 9 months vs. 10 for those with Metachronous metastasis patients ($P=0.018$).

KRAS status showed to have insignificant relation with PFS as patients with wild KRAS had progression free survival 9 months vs. 10 months for those with mutant one ($P=0.819$).

Among all patients who received anti-EGFR plus 5FU based chemotherapy vs. patients who did not receive anti-EGFR we conclude it had no significant relation with PFS as both groups had PFS 9 months ($P=0.838$).

Discussion

Colorectal (CRC) cancer incidence and mortality rates vary markedly around the world. Globally, colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with 1.8 million new cases and almost 861,000 deaths in 2018 according to the World Health Organization. Rates are substantially higher in males than in females. In the United States, both the incidence and mortality have been slowly but steadily decreasing (12).

In our study the mean age of the studied group was 58.70 ± 12.99 years, this was consistent with a descriptive cross-sectional hospital-based study in Egypt stated that The mean age was 51 ± 15 years (age range: 16–80 years) (13), but worldwide, the mean age was around 8 years younger than the mean age in our study (14).

Maybe this is due to late diagnosis in Egypt and better surveillance and diagnostic tools in the United States. Also it may be due to more consumption of carcinogenic materials in USA compared to Egyptian population due to lower social standards, CRC incidence and mortality rates have been declined in recent years, largely because of screening and surveillance programs that promote colonoscopy and stool testing in this population (15).

Sex distribution in our study showed that male to female ratio was 109/186 patients (58.6%) vs. 77/186 (41.4%) similar to data by the Austrian Society for gastroenterology and hepatology reported in JAMA, where men had higher rates of advanced colorectal tumors than women in all age groups, so males should start having screening colonoscopies at younger age than females (16).

Our study showed higher number of patients from urban residence 123/186 patients (66.1%) vs. 63/186 patients (33.9%) from rural residence, these findings were similar to Gharbiah cancer registry findings in Egypt which analyzed data of colorectal cancer since 1999 to 2007, stating that Colorectal cancer was more common in patients from urban (55%) than rural (45%) areas (17).

BMI of patients in our study was divided into normal 67/186 (36%) patients, abnormal 119/186 patients (64%) patients while a pooled analysis of individual data showed abnormal BMI patients were 41.5% vs. normal BMI 58.5% in colon cancer patients (18). This is due to differences in socioeconomic levels and nutritional habits.

Our study included 153/186 patients (82.3%) with performance status 1 vs. 33/186 patients (17.7%) with performance status 2, similar to a prospective Finnish nationwide study initiated in 2011, with 1086 mCRC patients enrolled, showed ECOG score 1 in (55%) and 2 in (18%) (19).

Initial CEA value in our study showed median CEA 6.25 ng/mL range (0–5659) at time of diagnosis, while a retrospective analysis of prospectively collected data. A total of 395 patients were radically treated for colorectal carcinoma showed that the average initial CEA levels were 7.51 ng/mL (0–157.6 ng/mL) (20). This difference may be due to the higher number of patients than our study.

In our study, out of 187 patients diagnosed with left colon cancer were 147/186 (79%) of patients and right colon cancer were 39/186 (21%). While a retrospective cohort study using the SEER database for identification of colon cancer from all the registries captured in the SEER 18 program diagnosis of colon cancers, (52.3%) were right-sided CC (RCC) and (47.7%) were left-sided CC (LCC) (21).

As regards the site of metastases in our study multiple site metastasis 91/186 (48.9%) were most common but if we consider single site metastasis liver comes in first place with 52/186 (28.0%) and bone metastasis come in last place with 3/186 (1.6%), these results were comparable to what was found by Van der Geest stating that the most common sites of metastases in metastatic colon cancer were liver (70%) and the least was in bone (12%) (22).

Synchronous metastasis in our study were found in 124/186 (66.7%) of patients while metachronous metastasis occurred in 62/186 (33.3%) of patients, while Hayashi M and his colleagues reported that 34% of patients with MCRC present with synchronous metastases (23). This may be due to late diagnosis of patients in our study compared to study documented by Hayashi and his colleagues.

Aggregate data from 4431 tumor samples from 12 data sources were included in the RAS mutation prevalence analysis. RAS mutation prevalence varied between data sources, ranging from 33.7% (95% CI: 28.4–39.3%) in the Middle Eastern pathology data set and to 53.6% (95% CI: 43.2–63.8%) and 54.1% (95% CI: 51.7–56.5%) in two European pathology centers (24), while in our study, patients who had RAS testing were 117 out of which 73 patients (62.3%) were wild-type while

44 (37.7%) were mutant, similar to our study Bazan and his colleagues reported that patients with CRC who underwent KRAS testing at Roswell Park Cancer Institute on 181 patients revealed the frequency of KRAS gene mutations was of 40% (25) Van Cutsem E. and his colleagues stated that BRAF mutations were 8% to 12% of patients with mCRC (26), while in our study out of 15 patients tested for BRAF mutation only 1 patient (6.6%) showed mutated type. This may be due to unavailability of BRAF testing for all patients.

Among whole patients in our study, 47/186 (25.3%) of patients received 5FU based chemotherapy plus anti-EGFR vs. 139/186 (74.7%) of patients received 5FU based chemotherapy alone.

Responses to treatment in our study occurred as follows, 97/186 (52.2%) of patients showed progressive course while 86/186 (46.2%) of patients showed stationary course and 3/186 (1.6%) of patients showed partial response, while in a retrospective, cohort study approved by the Institutional Review Board at a single outpatient cancer center showed that among metastatic colorectal patients who received treatment (50.7%) of patients experiencing a partial response and (20.0%) having stable disease and (29.3%) showed progressive course (27). This difference in response may be due to earlier diagnosis, better performance status in studied group and better following of treatment program and guidelines.

Median PFS in our study group was 9 months (ranged from 2-30) months, similarly a retrospective study analyzed 120 patients with MCRC, between January 2013 and March 2017 at the Medical Oncology Unit of the University of Palermo stated that the median PFS of the patients was 8.5 months (range 4–23 months) (28).

Median overall survival in our study was 18 months ranged from (2-51) months. While a retrospective study analyzed 120 patients diagnosed with pathologically confirmed MCRC, between January 2013 and March 2017 at the Medical Oncology Unit of the University of Palermo stated that median OS of 32.4 months (range 12–38.5) (28). This is due to different treatment received, different sequential treatment received upon progression and different number of patients.

Regarding body mass index relation to KRAS status there was no significant relation found between the two studied groups (mutant and wild) and BMI showing increase in percentage of overweight (41.1%) of patients vs. (38.6%) of patients in wild more than that in mutant groups respectively. While normal (38.6%) of patients vs. (38.4%) of patients and obese (22.7%) of patients vs. (20.5%) of patients showing higher percentages in mutant than wild groups respectively (P=0.950). This was similar to findings of a study done for all mCRC patients diagnosed between January 2012 and July 2017 at University Hospitals Coventry and Warwickshire were retrieved from a CRC database. There was no statistically significant association between BMI categories and KRAS status in any colon tumor location (29).

while Roswell Park Cancer Institute (RPCI) stated that the best overall response rate was 56.60% (27/53 PR and 3/53 CR) in KRAS WT and 50% (15/30 PR) in KRAS mutant patients (P=0.64). None of the patient with KRAS mutation had CR. Twenty-one patients (39.6%) had stable disease in KRAS WT and 15 (50%) in KRAS mutant patients (30).

In our study, wild group of patients had median progression free survival 9 months with range (2-30) months while it was 10 months with range (3-20) months in mutant group with no significant relation (P=0.544).

Consistent with a study for All patients with metastatic colorectal cancer at Roswell Park Cancer Institute (RPCI), the median PFS was 9.3 months (95% CI, 7.85 to 10.78) in KRAS WT and 8.7 months (95% CI, 5.42 to 15.18) in KRAS MT populations (P=0.395) (30).

Median overall survival in our study was higher in wild group with 20 months with range of (11-32 months) versus 18.5 months with range (12-24 months) in mutant group also with no significant difference (P=0.426).

Neelesh Sharma et al. (30). stated that Median OS was 34.8 months (95% CI, 23.5-42.5) in KRAS wild and not achieved in mutant patients (30). This is due to late diagnosis of patients in our study and higher incidence of synchronous metastasis and better selection of studied group in the other study.

People who are obese are slightly (about 30%) more likely to develop colorectal cancer than normal-weight people. A higher BMI is associated with increased risks of colon and rectal cancers in both men and in women, but the increases are higher in men than in women (31).

We classified patients in this study into normal group with BMI (18.5–24.9) and abnormal group with BMI more than or equal to 25 which known to include overweight and obese patients.

Our study showed normal BMI was found in younger age group with median age 55.6 years and range (22-75) years while abnormal BMI was noticed in older age group with median 60.4 years with range (27 – 81) years with significant relation (P=0.016), while the association between obesity and increased risk of overall CRC diagnosed at a median of over 63 years of age has been well documented (32).

Our study revealed that there was highly significant relation between BMI and sex as in normal BMI group there was 49/67 (73.1%) male patients vs. 60/119 (50.4%) in abnormal group, while females in normal group were 18/67 (26.9%) vs. 59/119 (49.6%) in abnormal group denoting increase number of both males and females in abnormal BMI group but with marked difference in female gender more than that of male (P=0.003).

While a recent meta-analysis found a higher risk of colon cancer for each 5-unit increment in BMI of 30% among men and 12% among women (33).

In our study, in normal weight group 43/67 (64.2%) of patients were living in urban areas vs. 80/119 (67.2%) of patients in abnormal group denoting higher BMI of patients in urban areas, while in normal group 24/67 (35.8%) of patients lived in rural areas vs. 39/119 (32.8%) in abnormal group with no significant difference (P=0.673). Another cohort study of Utah patients diagnosed with CRC was identified from the Utah Cancer Registry. Results showed that compared with urban men, rural CRC patients were diagnosed more overweight (34). This may be due to difference in food habits in different communities.

Lieke H.J and his colleagues analyzed CAIRO 2 study and found that patients with BMI <18.5 and ≥30.0 had a worse

performance status (35). While our study showed that relation between BMI and performance status was found insignificant, in normal group ECOG 1 were 60/67 (89.6%) patients vs. 93/119 (78.2%) in abnormal group, while performance status 2 in normal group was 7/67 (10.4%) vs. 26/119 (21.8%) (P= 0.051).

In our study, normal BMI group had median CEA 7 ng/mL with range (0.27 – 5659) while in abnormal group median CEA was 6 ng/mL with range (0.1 – 4164) with no significant difference (P=0.805). Similarly, a retrospective study was done, from January 2008 to December 2012, a total of 224 patients with stage IV CRC were treated. This study showed that BMI and carcino embryonic antigen (CEA) had a mild negative correlation, with a significant difference (R=-0.228, P=.001) (11).

In normal BMI group 52/67 (77.6%) of patients were with left colon cancer vs. 95/119 (79.8%) in abnormal group denoting higher incidence of abnormal BMI in left colon tumors, while in normal group 15/67 (22.4%) of patients were with right colon cancer vs. 24/119 (20.2%) in abnormal group with no significant value (P=0.721). Similarly, the association between colorectal cancer risk and BMI is, in general, stronger for cancers localized in the distal colon than other localizations. Concerning rectal cancer, some studies have shown scarce evidence for a connection with BMI (36).

In our study, multiple site metastasis patients were more in abnormal group 62/119 (52.1%) of patients vs. 29/67 (43.3%) in normal group BMI, while liver metastasis in normal group were 20/67 (29.9%) of patients higher than that in abnormal group 32/119 (26.9%), also lymph nodes metastasis incidence in normal group of BMI were higher 14/67 (20.9%) of patients vs. 8/119 (6.7%) patients in abnormal group, lung metastasis were more in abnormal BMI group 6/119 (5%) of patients vs. 1/67 (1.5%) in normal group, peritoneal deposits and adnexa were higher in abnormal BMI 8/119 (6.7%) of patients vs. 3/67 (4.5%) patients in normal group. Other metastasis (brain and bone) were found in abnormal group 3/119 (2.5%) of patients vs. no patients in normal group with significant differences (P=0.041), while descriptive statistics for the 21,149 patients analyzed showing that no clinical differences were observed in BMI distribution for patient and number of metastasis sites, presence versus absence of liver, lung, or lymph node metastases, colon versus rectal cancer, or therapy type (37).

Our study showed that in normal BMI group wild-type were 28/67 (41.8%) of patients vs. 45/119 (37.8%) in abnormal BMI group denoting higher incidence of wild KRAS in normal BMI group, similar to the results of Brändstedt J et al. (38) and dissimilar to results of Tabuso M. et al. (29).

Population-based cohort study Malmö Diet and Cancer Study (MDCS) stated that high BMI was significantly associated with BRAF wild patients (38), while our study showed correlation between BRAF status and BMI was insignificant, in normal BMI group 6/67 (9%) of patients were wild vs. 8/119 (6.7%) of patients in abnormal group denoting higher incidence of wild type BRAF in normal BMI group, while in abnormal group of BMI 1/119 (0.8%) of patients showed mutant BRAF while in normal group no patients showed mutant BRAF denoting higher incident of mutant BRAF in abnormal group, 61/67 (91.0%) of patients in normal group vs. 110/119 (92.4%) of patients in abnormal group were not reported with insignificant value (P=0.652).

A retrospective study was done, from January 2008 to December 2012, a total of 224 patients with stage IV CRC were treated showed that there were no statistically significant differences between pre-diagnosis BMI, and clinical response (P=.196) (11), while our study showed significant relationship, in normal BMI group 27/67 (40.3%) of patients showed progressive response to treatment vs. 70/119 (58.8%) in abnormal group denoting poorer response with abnormal BMI group. While in normal group 39/67 (58.2%) of patients showed stationary response vs. 47/119 (39.5%) in abnormal group denoting better response to treatment in normal BMI group, and partial response occurred in normal BMI group in 1/67 (1.5%) of patients vs. 2/119 (1.7%) in abnormal group with significant difference (P=0.048).

Our study showed that relation between BMI and progression free survival was insignificant showing in normal group BMI median PFS was 10 months with range (2-30) months vs. 9 months with range (2-24) months with no significant difference (P=0.402). Similar to results of a retrospective study done by Cong Z et al. (11)

A retrospective study included 224 patients with stage IV CRC showed OS of the high BMI group was significantly higher than that of the low BMI group (P=.002) (11), while our study revealed insignificant relation between them as in normal BMI group median overall survival was 19 months with range (2-46) months vs. 17 months with range (3-51) months with no significant difference (P=0.712). Another retrospective data were collected from the South Australian Clinical Registry for mCRC stated that patients treated with chemotherapy alone demonstrated no difference in median OS by BMI. Comparison of median OS for patients receiving chemotherapy alone versus chemotherapy and target therapy, within each BMI group demonstrated a survival benefit for the addition of target therapy in the normal group only (OS 21.0 vs. 35.7 months, HR 0.66, P value < 0.01) (39). These differences may be due to different modalities of treatment using anti-VEGF that improves outcome markedly in obese patients and anti-EGFR versus chemotherapy alone that was used in a group of patients in our study.

Our study showed that median overall survival in age group ≤59 years old was 30 months vs. 20 months for those above 59 years with no significant relation (P=0.162), while a study was done by Van Eeghen EE et al. (40) stated that age was significant predictors for overall survival (P<0.001) in cancer colon, while was not a significant predictors of survival in rectal cancer patients with median survival was 4.67 years. This difference may be due to larger sample size of the compared study (1575 patients).

A study done by the SEER registry showed that younger women (18–44 years old) with MCRC lived longer than younger men (17 months vs. 14, p<0.0001, log-rank test). In contrast, older women (55 and older) had significantly worse OS than older men (7 months vs. 9, p<0.0001.) (41), while our study showed no significant difference (p=0.230) in overall survival between males and females, for males was 24 months vs. 16 months for females.

Our study stated that patients of urban areas had median overall survival 23 months vs. 21 for those of rural areas with insignificant value (P=0.904). Similar to results of Rogers CR et al. (34).

In a study based on a pooled dataset from five clinical trials, patients with an ECOG score of 0 have better overall and progression-free survivals ($P < 0.001$) for both (42), while in our study, no significant correlation between median overall survival and performance status ≤ 2 ($P=0.375$). This may be due to different treatment protocols.

In our study, site of primary tumor revealed insignificant relation to overall survival in our study as patients of left colon cancer had median overall survival 23 months vs. those with right colon cancer had median overall survival 18 months with insignificant value ($P=0.241$), discordant with other results showing that 3-year survival revealing that right-sided primary CRC had inferior prognosis to both left-sided and rectal cancers (Deborah Schrag et al., (43); Byun JH et al., (44))

In our study, there is highly significant difference as patients who received previous treatment had median overall survival 39 months vs. 15 months for those who did not receive ($P=0.001$). Consistent with what was found by a pooled analysis for the role of adjuvant chemotherapy, patients who received 5-FU/LV chemotherapy after surgery improved the 5-year overall survival from 64% to 71% ($p = .001$) when compared to surgery alone (45).

Demographic data and clinical information were collected from 1,115 patients from the Republic of Korea, who presented with mCRC. Results showed that surgical resection of the primary tumor was associated with a more favorable prognosis. The median OS was 38.9 months (95% CI, 34.0 to 43.8) for patients who had undergone curative resection, 19.7 months (95% CI, 18.0 to 21.4) for patients who had undergone palliative resection, and 12.1 months (95% CI, 11.2 to 13.1) for patients who did not undergo surgical resection ($p = 0.007$) (44), while our study showed that patients with resected primary tumor had median overall survival 30 months vs. 11 months for those who did not had tumor resection ($P=0.001$).

Our study showed that there is a significant relation between site of metastasis and overall survival as patients with lymph nodes metastasis had median overall survival 39 months while those who had liver metastasis had median overall survival 24 months, other sites of metastasis (brain and bone) showed median overall survival 23 months, patients with multiple sites metastasis showed median overall survival 21 months, lung metastasis patients had median overall survival 19 months and patients with peritoneal deposits and adnexa had median overall survival 10 months ($P=0.021$), consistent with other studies which showed that the survival of patients with peritoneal metastasis was significantly poorer than the survival of patients with liver ($p < 0.05$), lung ($p = 0.002$), or extra-regional lymph node ($p = 0.001$) metastases. In contrast, no significant differences were observed for patients with bone or ovarian metastases ($p = 0.481$ and $p = 0.124$, respectively) and the median OS of patients with a single metastatic site, including those with a solitary metastasis, was significantly longer than that of patients with multiple metastatic sites ($p < 0.001$) (44).

A retrospective study investigated phase III CAIRO study results showed that no significant difference in median OS was observed between patients with synchronous metastases and metachronous metastases (17.6 vs. 18.5 months, respectively, $P=0.24$) (46), consistent with our study, in patients with synchronous metastasis showed median overall survival 15 months vs. 39 months for those with metachronous metastasis showing significant difference in favor of metachronous metastasis ($P=0.001$). This may be due to improper patients follow up in the compared study.

In our study, median overall survival of normal BMI was 26 months vs. 21 months for those with abnormal BMI group ($p=0.215$).

Similar to our results, retrospective data were obtained from the South Australian Registry for mCRC in which the OS was shorter for patients who were overweight compared to normal (OS 22.3 vs. 24.1 months, respectively, hazard ratio [HR] 2.21 and 1.23) (39).

In our study, BMI did not show significant correlation with progression free survival as normal BMI group had median progression free survival 10 months vs. 9 for those of abnormal BMI ($P= 0.481$), similarly a pooled analysis of individual data from 2085 patients enrolled in eight FFCD first-line mCRC trials from 1991 to 2013 was performed showing comparable median [progression-free survival](#) (PFS) (7.8 versus 7.2 months, HR = 0.96 [0.87–1.05] $p = 0.35$) for normal and abnormal respectively BMI group of patients (18). On the contrary, in a retrospective study from 4 oncological centers in Poland were included in the analysis, showed that Comparison of obese patient vs. overweight patients vs. normal patients BMI revealed a significant improvement of median PFS (9.4 vs. 9.1 vs. 7.3 months, $p = 0.03$) (47).

Conclusions:

patients with normal BMI achieved better results than those with abnormal BMI

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