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Radiological Response after Neoadjuvant Chemotherapy of Multiple and Bilobar Colorectal Liver Metastases

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Introduction: Surgical resection with or without ablation of liver metastases allows selected CRLM patients to achieve 5-year overall survival rates well above 50%. (Pulitano C et al, 2011)

Colorectal liver metastases (CRLM) are the commonest indication for hepatic surgery in the western world. Liver metastases affect between 30 and 50% of patients with colorectal cancer. (Zarour LR et al, 2017)

The administration of perioperative chemotherapy resulted in a 9.2% increase in 3-year PFS from 33.2% to 42.4% (P = 0.025), but no significant difference in OS . (Nordlinger B et al, 2013).

The Response Evaluation Criteria in Solid Tumors (RECIST) is used to objectively measure radiographic response to treatment for most solid organ cancers. However, conventional size-based RECIST criteria have been poor to predict pathologic response for CRLM (Shindoh J et al, 2012) . Modified criteria based on morphologic changes (mRECIST) has been superior to RECIST in assessing response to NCT, though neither were predictive of residual tumor burden (Egger ME et al, 2013).

Aim of the study: The aim of our study is to assess the radiological response to neoadjuvant chemotherapy and the correlation of radiological response to dosage and regimen of chemotherapy.

Methods: A prospective cohort study was performed, using the prospectively maintained database of twenty five patients have received neoadjuvant and undergoing liver resections for CRLM at national cancer institute in Cairo university between 2022 and 2024. Local ethical board clearance was obtained for this study.

Results: Twenty five patients were diagnosed with colorectal liver metastasis (CRLM) and are included in our cohort study. The mean age of patients is (45.8).

Rectum is the most common origin of colorectal liver metastases in (50 %). About (56 %) of patients have single large metastatic lesion , whereas (28%) of patients have multiple hepatic focal lesions (>= 3). Fourteen patients (56 %) have colorectal liver metastases equal to or more than 4 cm in the largest lesion.

Patients have received neoadjuvant chemotherapy and the regimen is ranging from three to nine cycles with average duration 5.5 months. Thirteen (13) patients have been treated with Xelox . However , other patients were given other regimens such as Folfiri and Xeloda, inaddition to combination with target therapy.

Ten Patients (40%) showed regressive course of the CRLM whereas eleven patients (44 %) have progressive course . The remaining four patients have shown a stationary disease .

Our results showed that the number of cycles of chemotherapy is directly proportional to the radiological response which is statistically significant (P = 0.043) . Also , patients who received longer duration of chemotherapy (> 6 months) , showed a better radiological response. It has been shown that locally advanced colon cancer (T4 N +ve) is associated with the worst radiological response to the neoadjuvant chemotherapy .On the other side , the earlier disease stage (T2 , T3 , N0) demonstrates a better response.

Finally, patients who have a radiological response developed a higher rate of recurrence (55.6 %) compared to patients who have a progressive disease on neoadjuvant chemotherapy. In addition, there are a better radiological response in patients (54.5 %) who have survived in the first year after surgery.

Discussion: The mean age of patients diagnosed with colorectal liver metastases in our cohort is 45.8 ± 15.7 which is much younger than in (Yao et al, 2021) in which the mean age is 57.48±9.55 years . This is mostly due to progressive trend of colorectal cancer in younger age.

In our study, the mean duration of neoadjuvant chemotherapy is 5.8 months and the majority of patients have received less than 6 months. Our results showed that longer duration of NAC (>= 6 months) is correlated with a better radiological response (p= 0.351) .In one report, administration of more than 12 weeks of chemotherapy and/or an interval of less than four weeks between chemotherapy and surgery was associated with increased postoperative complications, rates of reoperation, and longer hospital stay (Welsh FK et al, 2007) . In our results , The mean cycles of neoadjuvant chemotherapy is 5.6 cycles. However , the larger number of cycles (> = 6 cycles) is associated with a better radiological response (p = 0.043) ,

Other studies in the literature that showed there were no significant differences in R0 resection, pathological response or postoperative complications between the groups with a low number of NAC cycles group (≤5 cycles) and high number of NAC cycles (>5 cycles). Patients with a high number of NAC cycles were more likely to have NAC toxicity than those with a low number of cycles (Chen et al, 2021)

In our study , half of patients have been given Xelox and few patients (18.75 %) have received chemo-targeted chemotherapy. Our results, showed that combination chemotherapy (or chemo-targeted) developed a better radiological response (p = 0.843) . Also, In other studies patients who can tolerate a more intensive regimen, triplet therapy with FOLFOXIRI is an option that may lead to higher response rates. (Masi G et al, 2011) (p = 0.235).

After radiological assessment , 44 % of our patients showed progression on NACTH and the majority (56%) have a good response to NACTH in the form of RD (40%) and SD (16%). Both groups of patients show nearly similar recurrence rates but slightly higher in patients with a good radiological response. In the literature , clinical responses to neoadjuvant chemotherapy were complete response (CR, n = 1), partial response (PR, n = 24), stable disease (SD, n = 29), progressive disease (PD, n = 22) (Noda et al, 2023)

Conclusion: Neoadjuvant chemotherapy is considered as adjunct to surgery and can achieve downstaging of liver metastases that facilitates liver resection. Combination chemotherapy and chemo-targeted therapy leads to a higher disease response than single agent chemotherapy. Also , intense chemotherapy regimen regarding longer duration of chemotherapy or 6 cycles or more gives a higher disease response.

Keywords: neoadjuvant chemotherapy, radiological response, colorectal liver metastases.

1. Introduction

Colorectal liver metastases (CRLM) are the commonest indication for hepatic surgery in the western world. Liver metastases affect between 30 and 50% of patients with colorectal cancer. (Zarour LR et al, 2017) Historically, CRLM has been associated with a poor outcome and a 5-year overall survival rate as low as 5.3%. (Beppu T et al, 2014)

Surgical resection with or without ablation of liver metastases allows selected CRLM patients to achieve 5-year overall survival rates well above 50%. (Pulitano C et al, 2011)

25% of patients develop CRLM post CRC (colorectal cancer)resection, of which 25% are operable, and of which 25% are 10 year survivors, the difference in overall survival in a surveillance group may prove beyond detection. (Primrose JN et al, 2014)

Even among patients with initially resectable disease, downstaging with NCT could have certain advantages. Preoperative chemotherapy may facilitate a parenchymal-sparing or minimally invasive surgical approach, as well as increase the likelihood of obtaining negative margins. In addition, the use of NCT could lead to better selection of surgical candidates by allowing time to identify those who have rapidly progressive metastatic disease and therefore would not benefit from a potentially morbid operation. (Guo et al, 2021)

The administration of perioperative chemotherapy resulted in a 9.2% increase in 3-year PFS from 33.2% to 42.4% (P = 0.025), but no significant difference in OS . (Nordlinger B et al, 2013)

The Fong clinical risk score is arguably the most well-known algorithm to assess prognosis in patients with CRLM being considered for resection. It assigns a point for each of the following variables: positive margin, extrahepatic disease, node-positive primary, disease-free interval from primary to metastases < 12 mo, number of hepatic tumors > 1, largest hepatic tumor > 5 cm, and carcinoembryonic antigen (CEA) level > 200 ng/mL, as these factors were significant and independent predictors of poor long-term outcomes (Fong Y et al, 1999) . A variety of other models for clinical risk stratification have since been developed. Of note, in a study evaluating the accuracy of eight recognized scoring systems, including the Fong clinical risk score, only the Rees postoperative index was a significant predictor of disease-free and disease-specific survival at 1, 3, 5, and 10 years (Roberts KJ et al, 2014) .

The Response Evaluation Criteria in Solid Tumors (RECIST) is used to objectively measure radiographic response to treatment for most solid organ cancers. However, conventional size-based RECIST criteria have been poor to predict pathologic response for CRLM (Shindoh J et al, 2012) . Modified criteria based on morphologic changes (mRECIST) has been superior to RECIST in assessing response to NCT, though neither were predictive of residual tumor burden (Egger ME et al, 2013) .Optimal morphologic response to chemotherapy is defined as a change toward homogenous, hypoattenuating lesions with thin, sharply defined tumor-liver interface. While morphologic response correlates with pathologic response, the majority of treated CRLM (83%) that appear to have complete radiographic response to chemotherapy are subsequently found to have viable tumor on pathologic review (Shindoh J et al, 2012) (Benoist S et al, 2006)

2. Material and methods :-

A prospective cohort study was performed, using the prospectively maintained database of twenty five patients have received neoadjuvant and undergoing liver resections for CRLM at national cancer institute in Cairo university between 2022 and 2024. Local ethical board clearance was obtained for this study.

Inclusion criteria :-

- All patients have been diagnosed with colorectal cancer and have only liver metastases either synchronous or metachronous.

- All patients underwent resection of liver metastases either anatomical liver resection and non-anatomical resection.

- Patients were included in the final analysis if they underwent the first time surgery for CRLM. Patients undergoing simultaneous resections and two-stage procedures .

- Child score A liver patients.

- Liver metastases included: multiple, bilobar and single large lesion that require major resection.

Outcome Measures :-

- The primary outcomes were defined as

(1) Assessment of radiological response in patients who received neoadjuvant chemotherapy.

(2) Assessment of correlation between the radiological response and regimen , dose and type of neoadjuvant chemotherapy.

The secondary outcome is to assess the relation between the radiological response with the pathological response and the recurrence rate in one year after surgery.

Definitions:-

- Synchronous liver metastases :-

Liver metastases presented at the same time of colorectal cancer

- Metachronus liver metastases :-

Liver metastases presented after the appearance of colorectal cancer

- Non-anatomical liver resection :-

Surgical removal of liver metastases with margin independent on hepatic vasculature

- Anatomical liver resection :-

Surgical removal of liver metastases with margin with visualization of hepatic vasculature.

- Regressive disease :-

  Decrease in the number or size of the metastatic lesion according to RECIST criteria.

- Progressive disease :-

  Increase in the number or size of the metastatic lesion according to RECIST criteria.

Data Extraction :-

Our database was examined for baseline demographics, pre-operative clinical characteristics

(use of neoadjuvant chemotherapy, type , number of cycles inaddition to size and number of metastases before and after neoadjuvant chemotherapy) , intraoperative characteristics (type and extent of resection) and post-operative features (pathology , recurrence and survival in one year).

STATISTICAL METHODS:-

Statistical analysis was done using IBM SPSS® Statistics version 26 (IBM® Corp., Armonk, NY, USA). Numerical data was expressed as mean and standard deviation or median and range as appropriate. Qualitative data was expressed as frequency and percentage.

Comparison of quantitative variables between two groups was done using Mann-Whitney test (non-parametric t-test) for not normally distributed numerical data.

Correlation between numerical variables was tested using Spearman-rho correlation.

All tests were two-tailed. A p-value < 0.05 was considered significant.

3. Results :-

Twenty five patients were diagnosed with colorectal liver metastasis (CRLM) and are included in our cohort study. The mean age of patients is (45.8) and is ranging from 22 to 72 years. Male to female ratio is near to 1:1 . About (20 %) of patients have medical co-morbidities including diabetes mellitus , hypertension and cardiovascular complications.

Rectum is the most common origin of colorectal liver metastases in (50 %) . About (56 %) of patients have single large metastatic lesion , whereas (28%) of patients have multiple hepatic focal lesions (>= 3). Fourteen patients (56 %) have colorectal liver metastases equal to or more than 4 cm in the largest lesion.

Patients have received neoadjuvant chemotherapy and the regimen is ranging from three to nine cycles with average duration 5.5 months. Thirteen (13) patients have been treated with Xelox . However , other patients were given other regimens such as Folfiri and Xeloda, inaddition to combination with target therapy.

Following neoadjuvant chemotherapy , fourteen (60.8 %) patients have more than one lesion , but (39.2 %) of all patients have single lesion. On the other side , twelve patients (60%) have colorectal liver metastases equal to or more than 4 cm in the largest diameter.

Ten Patients (40%) showed regressive course of the CRLM whereas eleven patients (44 %) have progressive course . The remaining four patients have shown a stationary disease . Seven patients (28%) have received preoperative TACE (transarterial embolization) but no one of them have showen a radiological response. Seven patients have received TACE , but with no any reported response.

The majority (89.5 %) of the patients were diagnosed with colonic adenocarcinoma Grade 2. However , only two patients have grade 3 colonic adenocarcinoma. After colorectal resection , the majority of patients have T3 colonic staging and node positive patients represent about 48 % of patients.

A seventeen patients (68 %) underwent colon first approach , while the remaining eight

patients underwent concomitant resection of the liver and colon. Eighteen patients (72 %) underwent non-anatomical resection . Other seven patients underwent anatomical resection including formal hepatectomy and segmentectomy. Only two patients underwent hepatectomy in two stages.

Pathological analysis after liver resection showed that the size of largest lesion is 4 cm or more in (66.6 %) of cases. The average size of the largest liver metastases is 4.5 cm . (52%) of patients showed that a surgical margin more than 1 mm – 4 mm for the excised lesions . Only 4 patients who have a pathological response to neoadjuvant chemotherapy in the form of partial response in 3 patients and one patient had showed pathological complete response.

Only five patients who have been demonstrating post-operative morbidity in the first month . Two patients had bile leakage manifested in drains and intestinal leakage , post-operative bleeding and obstructive jaundice were present in the last three patients . During follow-up in one year , recurrence has been reported in (75 %) of patients which is present mainly in liver in the majority of patients. Only one patient who died in the first year.

Table 1 :- epidemiological factors

		Number	Percent
Age (years)	Mean ±SD	45.8±15.7	
Gender	Male	13	52
	Female	12	48
Presence of Comorbidity	yes	5	20
	No	20	80
Site of the primary cancer	Rectum	12	50
	Left sided	11	41.6
	Right sided	1	8.3
Number of metastases (before NACTH)	Single	14	56
	Two	4	16
	Multiple	7	28
Size of the largest metastases (before NACTH)	< 4 cm	11	44
	>= 4 cm	14	56
	Mean	4.5	
Type of chemotherapy	Xelox	13	52
	Other chemotherapeutic agents	5	28
	Combination of chemotherapy with target therapy	5	20

Number of cycles	(range)	(3-9)	
	Mean	5.2	
Duration of CTH (months)	Mean (range)	5.5 (3 - 21)	
Number of metastases post NACTH	Single	9	39.2
	Double	7	30.4
	Multiple > 3	7	30.4
Size of the largest lesion post NACTH	< 4 cm	10	40
	>= 4 cm	12	60
Radiological response	Regressive	10	40
	Stationary	4	16
	Progressive	11	44
Grade	II	17	89.47
	III	2	10.53
Colonic T staging	T2	4	16.6
	T3	16	66.7
	T4	4	16.6
Colonic N staging	Nx	3	12
	N0	10	40
	N1,2	12	48
Approach of resection	Colon first	17	68
	Concomitant	8	32
Type of surgery	Non-anatomical	18	72
	Anatomical hepatectomy	6	24
	Anatomical segmentectomy	1	4
Size of largest lesion in pathological analysis	< 4 cm	8	33.33
	>= 4 cm	16	66.7
Margins	Mean	4.5	

	< 1mm	4	16
	1 mm – 4 mm	13	52
	4 mm – 9 mm	4	16
	>1cm	4	16

Table 2:- postoperative parameters for patients diagnosed with CRLM

		Number	Percent
Pathological response	No response	17	68
	Partial response	7	28
	Complete response	1	4
Post-operative morbidity or mortality in one month	No	18	75
	Morbidity and mortality	6	25
Two stage hepatectomy	Yes	2	8
	No	23	92
Additional therapy	No	18	72
	TACE	7	28
DFS in one year		6	25
	Yes (Disease free)	18	75
	No (recurrence)		
Survival in one year	Yes	22	95.6
	No	1	4.4

Correlation between the radiological response and other parameters

After neoadjuvant chemotherapy had been given , radiological response was elicited (by change in the size and/or number of liver metastases) . Finally, we have two groups of patients . Fourteen patients have shown radiological response (including stationary disease (SD) and regressive disease (RD)). Other eleven patients showed progressive disease (PD) .

Table (3) correlation between radiological response and other pre-operative parameters :-

		Radiological response				
		RD + SD (n=14)		PD (n=11)		
		Number	Percent	Number	Percent	p value
Age (yrs)	-Mean ±SD	45.9 ±12.1		45.7±15.7		0.622
Gender	-Female	7	58.3	5	41.7	0.821
	-Male	7	53.8	6	46.2	
Initial Size of the largest lesion	-< 4 cm	4	36.4	7	63.6	0.080
	->= 4 cm	10	71.4	4	28.6	
	- Mean ±SD	5.4 ±3		3 ± 1.4		
Initial Number of liver metastases	-single	6	42.9	8	57.1	0.135
	-Multiple	8	72.7	3	27.3	
Duration of chemotherapy	-< 6 months ->= 6 months	9 5	56.3 83.3	7 1	43.8 16.7	0.351
	- Mean ±SD	7.8±6.3		3.2 ± 1.6		
Type of chemotherapy	-Xelox/folfiri	7	53.8	6	46.2	0.843
	-Combination chemotherapy and target	4	80.0	1	20.0	
	- Single agent	3	60.0	2	40.0	
Number of cycles	-<6 ->= 6 - Mean ±SD	3 9 6.6± 1.5	37.5 90.0	5 1 3.8± 1.2	62.5 10.0	0.043

Patients who have the initial tumor size larger than 4 cm showed a better radiological response to neoadjuvant chemotherapy than smaller tumors < 4 cm (p = 0.080) as shown in figure (1) .

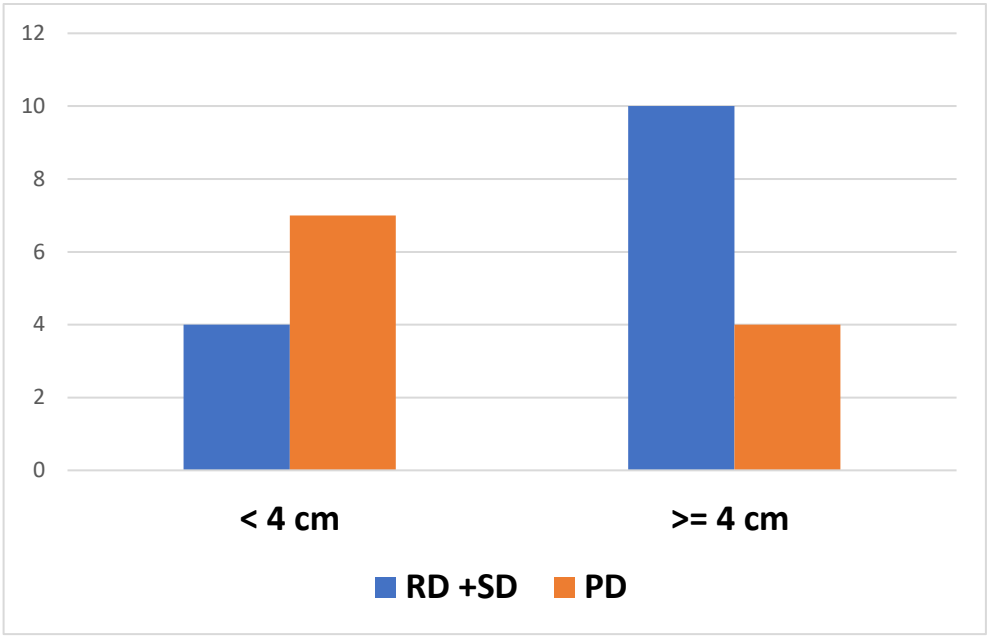

Figure (1) the relation of initial tumor size to the radiological response to the neoadjuvant chemotherapy.

In addition, patients who have multiple tumors in initial assessment showed a better radiological response than fewer number of metastasis or single lesion (as demonstrated in Figure (2) .

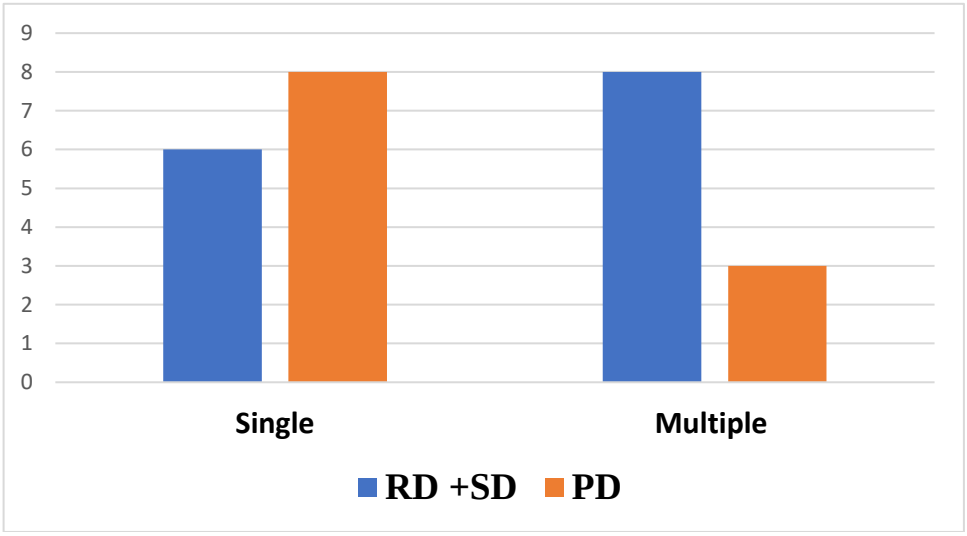

Figure (2) showing the relation between the number of liver metastases and the radiological response.

Our results showed that the number of cycles of chemotherapy is directly proportional to the radiological response which is statistically significant (P = 0.043) . Also , patients who received longer duration of chemotherapy (> 6 months) , showed a better radiological response.

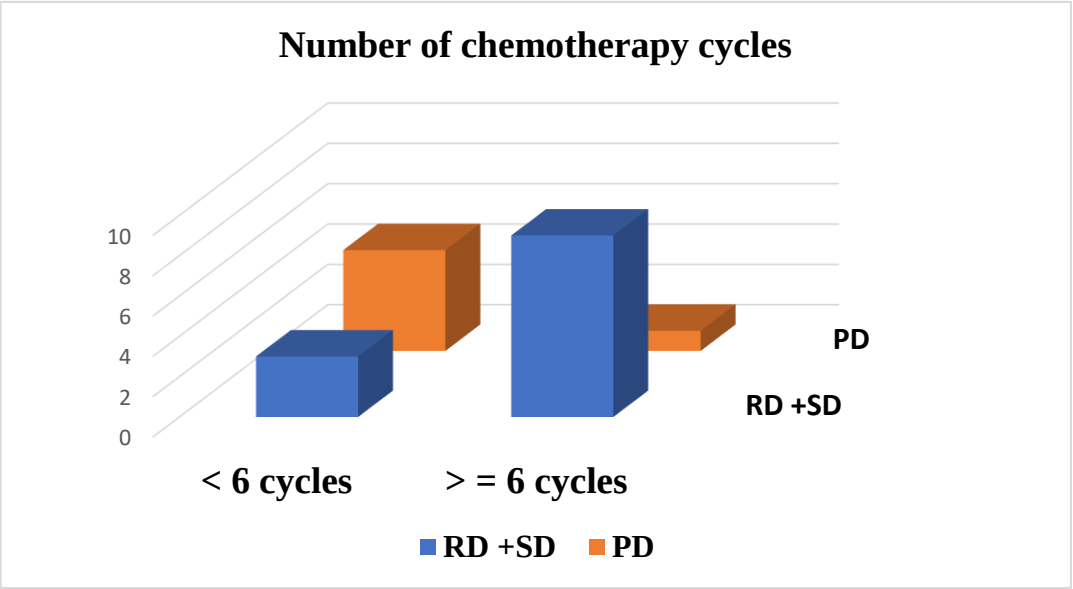

Figure (3) showing the relation between the number of chemotherapy cycles and the radiological response.

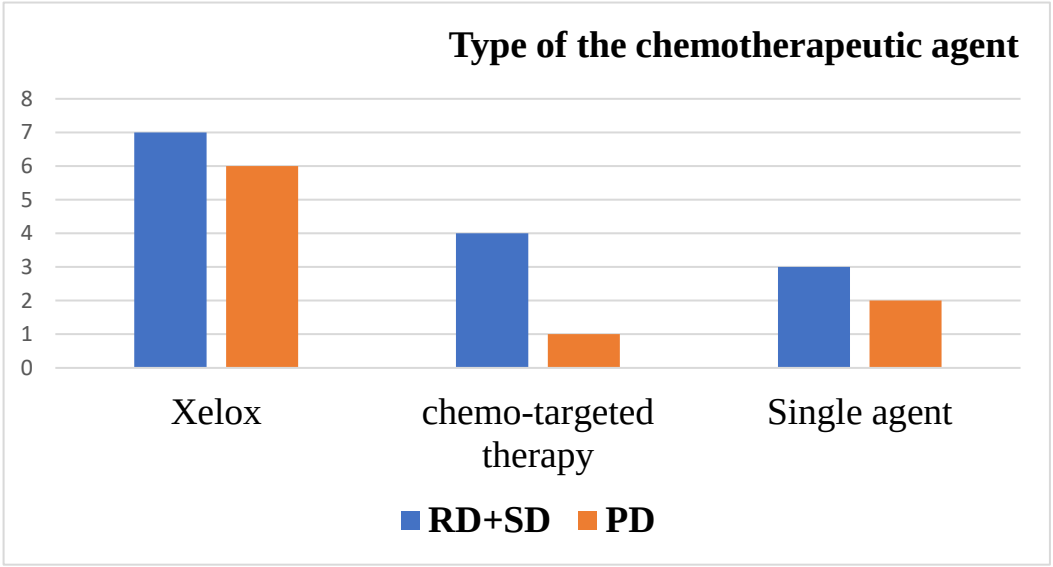

Figure (4) showing the relation between the type of chemotherapeutic agent and the radiological response.

Our results revealed that the administration of chemo-targeted therapy is associated with

higher radiological response than the use of single agent (P = 0.843) .

Table (4) correlation between radiological response and other operative and post-operative parameters :-

		Radiological response				
		RD + SD (n=14)		PD (n=11)		
		Number	Percent	Number	Percent	p value
Pathological T	-T2	3	75.0	1	25.0	0.434
	-T3	9	56.3	7	43.8	
	-T4	1	25.0	3	75.0	
Pathological N	-N0	7	70.0	3	30.0	0.231
	-N 1,2	5	41.7	7	58.3	
Tumor size in final pathology	-< 4 cm	4	50.0	4	50.0	1.000
	->= 4 cm	9	56.3	7	43.8	
	- Mean ±SD	4.5 ±3.5		4.5 ± 1.8		
Pathological response						
	-No response	9	52.9	8	47.1	
	-Partial response	4	57.1	3	42.9	
Recurrence	- PCR	1	100.0	0	0.0	
	-No	3	50.0	3	50.0	1.000
Survival in one year	-Yes	10	55.6	8	44.4	
	-Yes	12	54.5	10	45.5	
	-No	1	100	0	0.0	

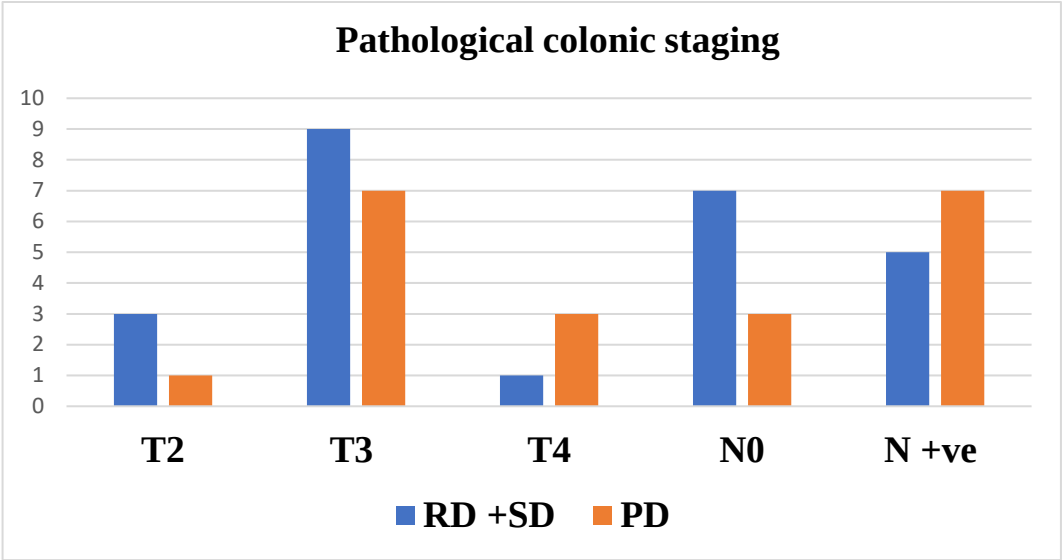

Figure (5) showing the relation between the colonic TN staging and the radiological response.

It has been shown that locally advanced colon cancer (T4 N +ve) is associated with the worst radiological response to the neoadjuvant chemotherapy .On the other side , the earlier disease stage (T2 , T3 , N0) demonstrates a better response.

Our results haven't shown any direct relation between the radiological response and either the pathological response to chemotherapy .

Finally, patients who have a radiological response developed a higher rate of recurrence (55.6 %) compared to patients who have a progressive disease on neoadjuvant chemotherapy. In addition , there are a better radiological response in patients (54.5 %) who have survived in the first year after surgery.

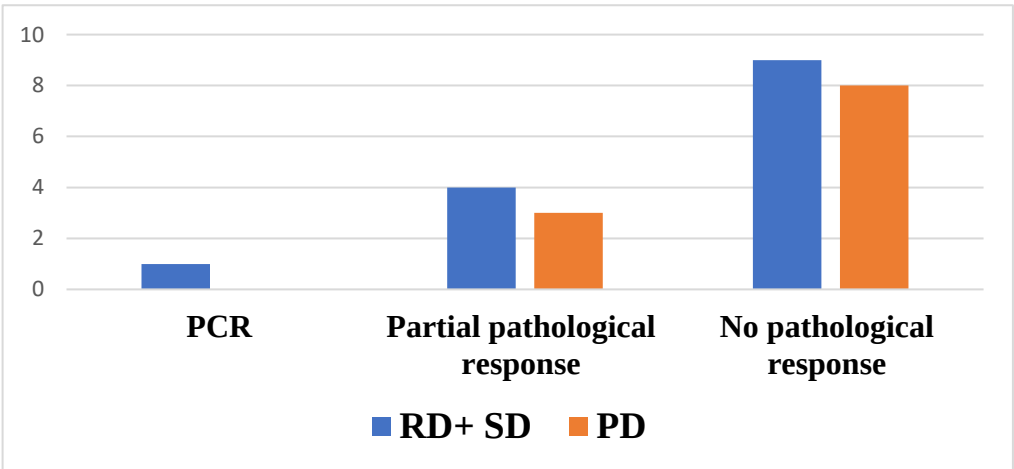

Figure (6) showing the relation between the pathological response and and the radiological

response .

4. Discussion :-

The mean age of patients diagnosed with colorectal liver metastases in our cohort is 45.8 ± 15.7 which is much younger than in (Yao et al, 2021) in which the mean age is 57.48±9.55 years . This is mostly due to progressive trend of colorectal cancer in younger age.

Initially in our results , The majority of liver metastases (58.5 %) are (>= 2) in number . The multiplicity of liver metastases is associated with a better radiological response (SD +RD) than single lesion (p = 0.135) .In other studies , only an initial number of metastases exceeding three lesions is independent predictive factor for the occurrence of DLM or a good radiological response (Gaujoux et al, 2011) . This is due to the fact that neoadjuvant chemotherapy has a dramatic effect on a huge tumor volume.

On initial assessment of our patients , The average size of the largest liver metastases is 4.5 cm and about 59.5% of patients have liver metastases equal or larger than 4 cm. This group of patients have a better radiological response than smaller tumors (< 4cm) (p =0.80). This is similar to Zhou et al which reported that patients with larger tumors tended to have a better regression. Only (3.4%) of patients with > 5-cm lesion progressed, whereas (18.0%) of patients with a < 5-cm metastasis progressed after chemotherapy (Zhou, et al 2022) . In Viganò et al , the early recurrence rate (at 3 months) was 44.4% of those with ≥ 15 metastases (Viganò et al, 2022) . Again , this is most likely due to the effect of neoadjuvant chemotherapy on huge tumor volume.

In our study , the mean duration of neoadjuvant chemotherapy is 5.8 months and the majority of patients have received less than 6 months. Our results showed that longer duration of NAC (>= 6 months) is correlated with a better radiological response (p= 0.351) .In one report, administration of more than 12 weeks of chemotherapy and/or an interval of less than four weeks between chemotherapy and surgery was associated with increased postoperative complications, rates of reoperation, and longer hospital stay (Welsh FK et al, 2007) . In our results , The mean cycles of neoadjuvant chemotherapy is 5.6 cycles. However , the larger number of cycles (> = 6 cycles) is associated with a better radiological response (p = 0.043) ,

Other studies in the literature that showed there were no significant differences in R0 resection, pathological response or postoperative complications between the groups with a low number of NAC cycles group (≤5 cycles) and high number of NAC cycles (>5 cycles). Patients with a high number of NAC cycles were more likely to have NAC toxicity than those with a low number of cycles (Chen et al, 2021)

In our study , half of patients have been given Xelox and few patients (18.75 %) have received chemo-targeted chemotherapy. Our results, showed that combination chemotherapy (or chemo-targeted) developed a better radiological response (p = 0.843) . Also, In other studies patients who can tolerate a more intensive regimen, triplet therapy with FOLFOXIRI is an option that may lead to higher response rates. (Masi G et al, 2011) (p = 0.235).

After radiological assessment , 44 % of our patients showed progression on NACTH

and the majority (56%) have a good response to NACTH in the form of RD (40%) and SD (16%). Both groups of patients show nearly similar recurrence rates but slightly higher in patients with a good radiological response. In the literature , clinical responses to neoadjuvant chemotherapy were complete response (CR, n = 1), partial response (PR, n = 24), stable disease (SD, n = 29), progressive disease (PD, n = 22) (Noda et al, 2023) .The combination of 5FU with oxaliplatin typically FOLFOX or XELOX (capecitabine and oxaliplatin) and irinotecan typically FOLFIRI or XELIRI (capecitabine and irinotecan), has yielded overall response rate (ORR) of between 20-30% to 40-50%. However, the FOLFOX first was associated with a higher complete response rates (CRR) than FOLFIRI (4.5 vs. 2.8%). (Ismaili et al, 2011)

Our study showed that T2 is more commonly associated with a better radiological response of liver metastases than other colonic staging (p = 0.434). Similarly , N0 is associated with a better radiological response (p = 0.231). In the literature , In regard to clinical N staging, patients in the non-disease responsive group primarily were staged to be N1 (52.8%), while stage N2 (73.5%) ranked the top in the disease responsive group.(Ma et al, 2021).

Patients in our study who had a good radiological response (SD + RD) have a higher rate of recurrence than who showed a progressive disease . This is most likely related either to the aggressive disease biology and proved that there is no actual relation between the clinical response and the disappearance of the disease in the liver . In other studies , median disease-free survival was 16 months (95% CI 10.8–22.7 months) in rad-responders and 12 months (95% CI 8.1–18.2 months) in rad-non responders, respectively (Brouquet et al, 2020) .The patients with resected DLM (disappearing liver lesion) had lower incidence of intrahepatic reoccurrence (69 and 35% 1- and 3-year disease-free survival vs. 40 and 16%) .Patients with resected DLM had a longer disease-free survival compared to patients with DLM left in situ but statistically significant differences in overall survival could not be found (Martin et al, 2020)., Patients with response to neoadjuvant chemotherapy had better survival than those with stable or progressive disease (5-y OS: 65% vs. 50%; 5-y DFS: 20% vs. 10%) (Berardi et al, 2018).

5. Conclusion :-

Multiple and bilobar colorectal liver metastases could be resected with an accepted outcome regarding the disease free survival and overall survival. Surgical management is still the definitive treatment for colorectal liver metastases that can achieve best overall survival. Neoadjuvant chemotherapy is considered as adjunct to surgery and can achieve downstaging of liver metastases that facilitates liver resection. However , the radiological response had no an impact on disease recurrence. Combination chemotherapy and chemo-targeted therapy leads to a higher disease response than single agent chemotherapy. Also , intense chemotherapy regimen regarding longer duration of chemotherapy or 6 cycles or more gives a higher disease response.

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