P353-Colorectal cancer liver metastases challenges and potential opportunities Systematic review and meta-analysis

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BACKGROUND

Colorectal cancer liver metastases (CLMs) occur in 25%-30% of CRC patients which represent heterogeneous cohort of patients based on the extent of the disease and the eligibility for resection. Resectable liver confined metastasis is the best scenario as surgery can offer cure with 5 year survival about 40%. The caveat is that only 25% of CLMs are initially resectable so preoperative treatment could confer conversion of unresectable and borderline CLMs into respectability. Practical speaking, there are no guidelines that help clinical decision in management of CLMs as regard resectability criteria and best systemic treatment to be used.

OBJECTIVES

1-Compare different chemotherapeutic regimens given preoperatively to CLM patients regarding response rate and R0 resection rate in different case scenarios if resectable, borderline and unresectable.
2- Determine the role of targeting agents in the conversion therapy strategy.
3- Investigate if there is correlation between response rate and R0 resection rate, to investigate the prognostic effect of RR over R0 rate.

MATERIAL & METHODS

Literature search of Scopus and Ovid databases was conducted to identify studies of perioperative systemic treatment in liver confined resectable and unresectable CLMs. The analysis was stratified according to study design either RCTs or single arm cohort studies and systematic review was performed of all identified studies. SPSS version 20 was used to calculate overall response rate (RR), resection rate R0 and correlation between RR and R0.

RESULTS

From 1440 articles initially retrieved, 28 studies were included in the analysis, of them 8 were RTCs and 20 were cohort studies so were analyzed in two separate analyses.
In **resectable CLMs** , EORTC 40983 showed that the RR was 43% for FOLFOX4 preoperatively with same R0 rate when compared to upfront surgery. FOLFOX4 was also used in 3 cohort studies and achieved higher RR and R0 when compared with other regimens. Anti-EGFR MoAbs combination with chemotherapy results in detrimental effect when used preoperatively in one RCT and one cohort study.
For **unresectable CLMs**, chemotherapy alone was used in 6 studies and Irinotecan based regimen achieved the highest R0 rate 33%. Bevacizumab was used in two trials with conversion rate 42% when combined with CAPOX. Cetuximab was used in 7 studies and achieved the highest RR and R0 79.7%, 80% respectively.

CONCLUSIONS

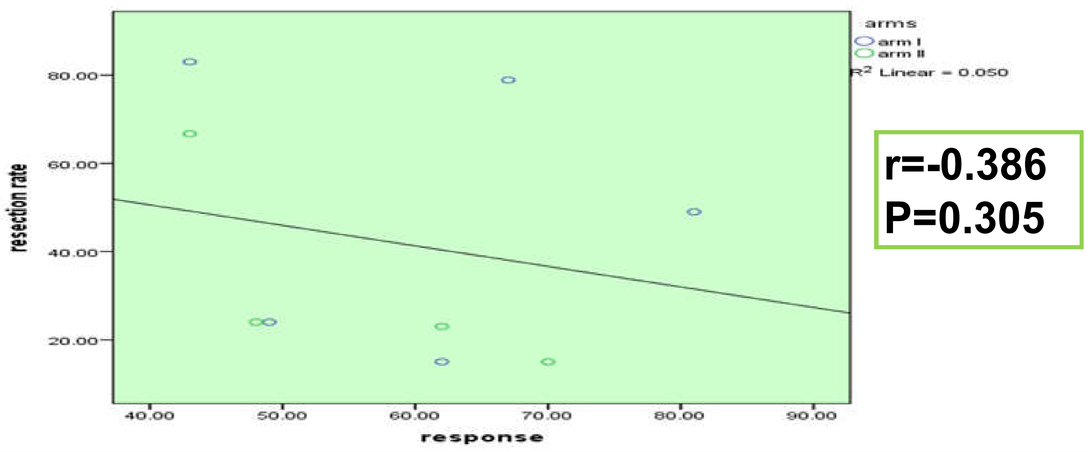
For initially resectable CLMs, surgery is the cornerstone for treatment albeit the question about the value of preoperative chemotherapy in absence of clear survival benefit.
In unresectable CLMs, achieving higher RR using targated agents correlates with higher R0 rate but further RTCs are needed to investigate the significant effect of on survival.

RESULTS OF 8 RCTS

Table (1) Impact of type of treatment protocols on resection rates

Treatment protocols	Resection rate (%)	
	Arm I	Arm II
-Chemotherapy alone	40.67	56.67
-Upfront surgery	59.6	84.0
-Chemotherapy + Cetuximab	---	15.0
-Chemotherapy + Bevacizumab	63.95	23.0
P value	**0.734**	**0.464**

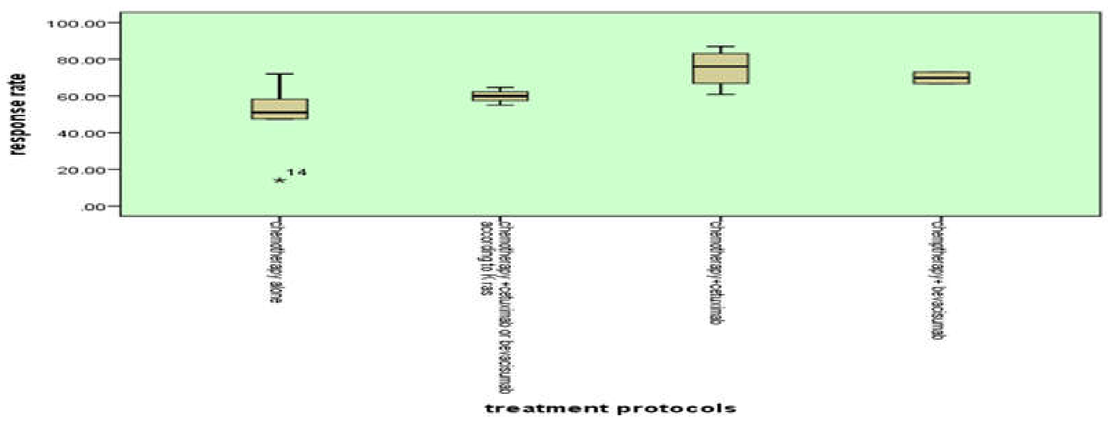
Figure (1) The correlation between the overall response rate and the resection rate



r=-0.386
P=0.305

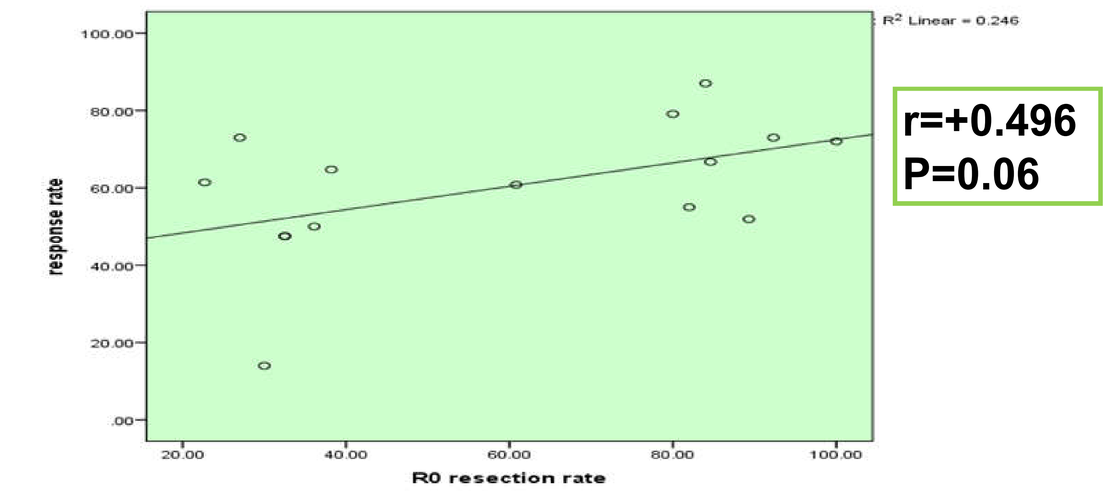
RESULTS OF 20 COHORT STUDIES

Figure (2) The relation between the mean response rate and the treatment used



The highest response rate was achieved by chemotherapy + Cetuximab protocol followed by chemotherapy + Bevacizumab, then chemotherapy wither either Cetuximab or Bevacizumab, and finally chemotherapy protocols, **P=0.048**

Figure (3) The correlation between the response rate and the R0 resection rate



r=+0.496
P=0.06

REFERENCES

References provided upon request