PRE-OPERATIVE HISTOLOGICAL PARAMETERS AS A PREDICTOR OF CHEMOTHERAPY RESPONSE IN ADVANCED OVARIAN CANCER

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Introduction

Ovarian cancer is the second deadliest gynecological worldwide as most women present with advanced-stage disease. There is also no strong consensus as to which women will benefit most from neoadjuvant chemotherapy and interval debulking, but it is usually preserved for the poor candidates for primary surgery due to either the location or severity of the disease or medical comorbidity. Multiple factors such as age, ethnicity, histological type, Stage, FIGO stage, residual disease, CA125 level and health status at the time of diagnosis affect the survival of cancer ovary. The Ki-67 protein is linked with malignancy, tumor aggression, reserved prognosis and metastases. Ovarian cancer response is assessed by the Chemotherapy Response Score(CRS) which is a three-tier score that stratifies patients into complete (CRS3), partial (CRS2), and minimal (CRS1) response based on examination that was described by Bohm et al.

Aim of the work

To evaluate the clinical and pathological parameters that predicts the response to neoadjuvant chemotherapy.
To validate and refine the Chemotherapy Response Score.

PATIENTS

All The women (n = 22) who presented to Al-Shatby University Maternity Hospital and Alexandria University Pathology and Clinical Oncology Departments 2017-2019 who were diagnosed with advanced ovarian cancer, had two years of follow up, and took Neoadjuvant chemotherapy.
The exclusion criteria were:Women with non-epithelial types of ovarian cancer,Undifferentiated carcinoma of the ovary,Women who had primary Cytoreductive Surgery and adjuvant chemotherapy,Women with stage I and II ovarian cancer,Women with Krukenberg tumor.

Methods

The study was retrospective review of the patients. Patients data were collected. Pre-chemotherapy core-biopsy paraffin blocks were examined under the microscope and stained with Ki-67 tumor marker. Chemotherapy regimes were documented and operative data were collected. Post-operative paraffin blocks were examined for chemotherapy response assessment. A two year follow up (Overall survival and progression free survival) data was recorded.

Results

The results showed significant association between good response to chemotherapy and younger age, lower FIGO Stage, Higher Ca-125, Higher Grade Serous carcinomas, Higher Ki 67 and the presence tumor infiltrating lymphocytes. We also validated and refined the Chemotherapy Response Score CRS and found it significantly associated with progression free survival and Overall survival.

Table :Relation between Chemotherapy Response Score with Histopathological parameters in pre-chemotherapy (n = 22)

	CRS score						Test of Sig.	p
	1 - No response (0 – 4) (n = 3)		2 - Partial response (5 – 11) (n = 11)		3 - Complete response (12 – 14) (n = 8)			
	No.	%	No.	%	No.	%		
Histological type								
Serous	3	100.0	7	63.6	7	87.5		
Mucinous tumors	0	0.0	2	18.2	0	0.0	χ^2= 2.597	^{MC}p= 0.752
Endometrioid tumor	0	0.0	2	18.2	1	12.5		
Grade								
Low	0	0.0	6	54.5	0	0.0	χ^2= 7.244*	^{MC}p= 0.027*
High	3	100.0	5	45.5	8	100.0		
KI-67								
Min. – Max.	7.0 – 25.0		3.0 – 40.0		12.0 – 90.0		H= 10.999*	0.004*
Mean ± SD.	17.33 ± 9.29		17.36 ± 11.65		62.25 ± 29.18			
Median	20.0		12.0		65.50			
Tumor infiltrating lymphocytes								
Absent	1	33.3	0	0.0	0	0.0		
+1	2	66.7	9	81.8	0	0.0	χ^2= 18.809*	^{MC}p <0.001*
+2	0	0.0	2	18.2	4	50.0		
+3	0	0.0	0	0.0	4	50.0		

SD: **Standard deviation**
χ^2: **Chi square test**
p: p value for comparing between different responses
*: Statistically significant at p ≤ 0.05
H: H for **Kruskal Wallis test**
MC: **Monte Carlo**

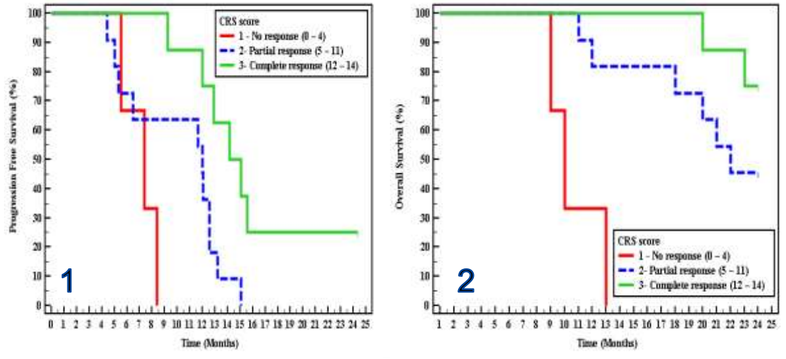

Figure (1): Kaplan-Meier survival curve for progression free survival with Chemotherapy Response Score
Figure (2): **):** Kaplan-Meier survival curve for overall survival with Chemotherapy Response Score

Conclusion

A variety of factors are thought to affect response to chemotherapy in ovarian cancers. We found that the lesser the stage of cancer, the better response to NACT. The higher grades of the cancer with higher KI 67 expression are more chemo-sensitive than lower grade. Epithelial ovarian cancer with higher concentration of tumor infiltrating lymphocytes had better chemotherapy response.
Ki-67 LI helps predict prognosis of high grade ovarian cancer, predicting the reaction to chemotherapy however the relation with overall survival needs further assessment.
The refined Chemotherapy Response Score was proved a valid tool to evaluate response to NACT as it correlated well with progression free interval and overall survival.