To assess the relationship between chemotherapy response score and homologous recombination deficiency status in patients with high-grade serous ovarian carcinoma.

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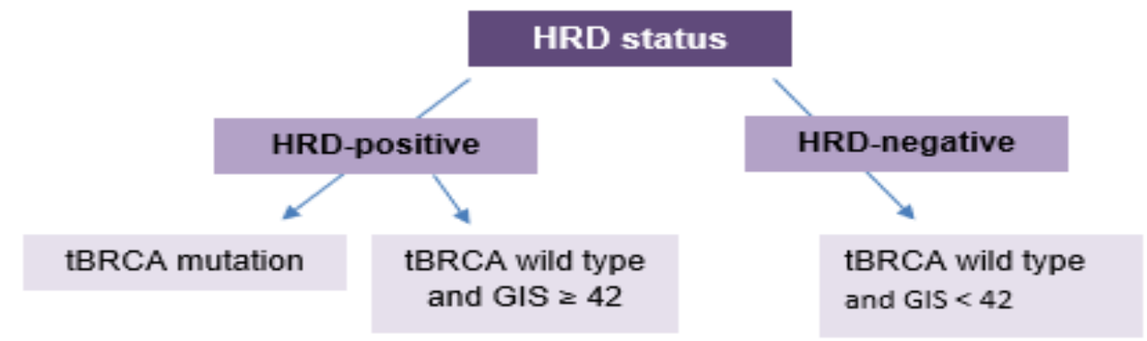
Introduction

High-grade serous ovarian carcinoma (HGSOC) is the most common histological subtype of ovarian cancer. [1-2]

The standard treatment for HGSOC at UCLH is neoadjuvant chemotherapy (NAC) followed by interval debulking surgery (IDS).

Homologous recombination deficiency (HRD) tumours are defined as those that either show tumour mutations in BRCA 1 or 2 and/or genomic instability score (GIS) of ≥ 42. [3]



HRD tumours have been shown to have increased sensitivity and response towards chemotherapy.[3]

The Cancer Genome Atlas (TCGA) project revealed that ~50% of HGSOC showed HRD.[4]

Response of HGSOC towards NAC is graded using chemotherapy response score (CRS) system[5] which is a histopathological assessment of tumour regression based on omental examination of IDS specimen (Figure 1).

Higher CRS has been associated with improved progression-free survival (PFS).[5]

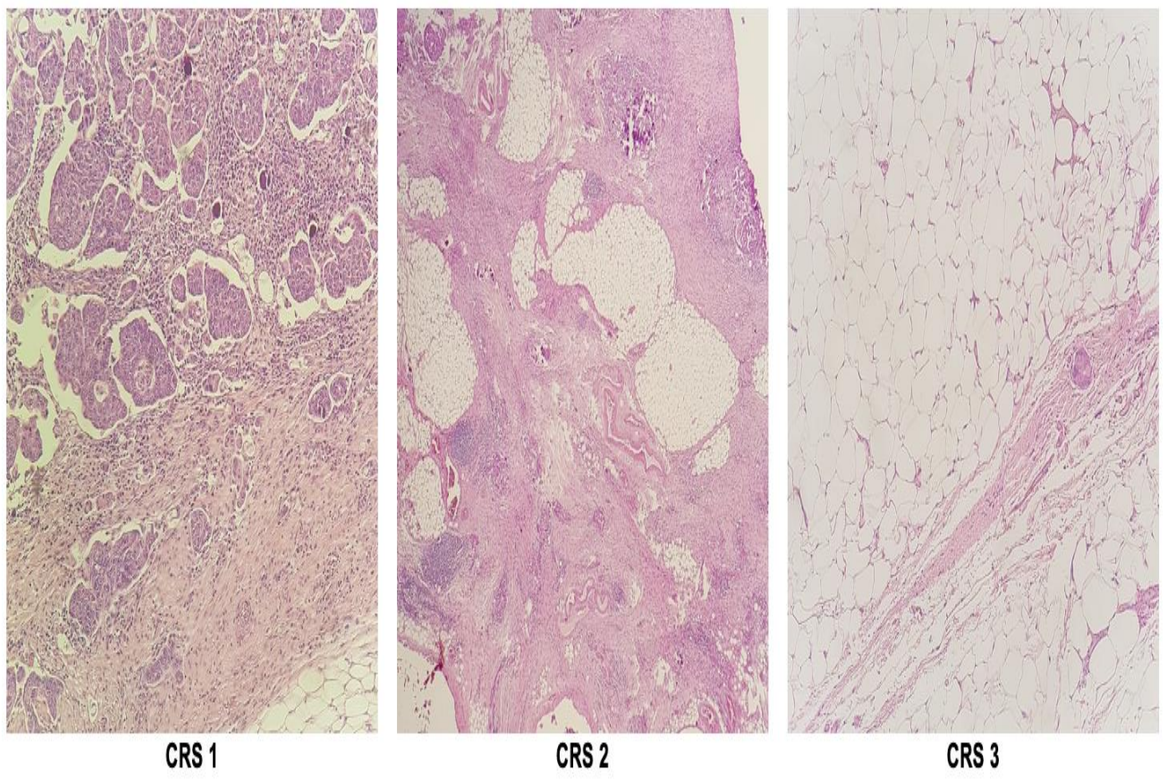


Figure 1: No or minimal response (CRS1), partial (CRS2) and complete or near complete (CRS3).

Aims

We investigated the correlation between HRD tumours, germline BRCA1/2 (gBRCA1/2) mutation and CRS.

Methods

We examined 37 HGSOC cases that received NAC prior to the IDS. The HRD and gBRCA status were determined and assessed against the CRS from the IDS.

Results

Of 37 cases, **15** (41%) were HRD tumours (12 GIS≥42, 9 tBRCA1/2 mutation; 6 had both GIS≥42 and tBRCA1/2 mutations, and 7 had concurrent gBRCA1/2 mutation). **19** (51%) were non-HRD tumours.

HRD tumours status (both GIS≥42 and tBRCA1/2) were not available in **3** (8%) cases, but 2 of those showed gBRCA1/2 mutation.

HRD status	Total	GIS≥42	tBRCA1/2 mutation	GIS≥42 and tBRCA 1/2 mutation	gBRCA1/2 mutation
HRD tumours	15	12	9	6	7
Non-HRD tumours	19	0	0	0	0
HRD status not available for both GIS and tBRCA1/2 mutation	3	-	-	-	2

Table 1: Frequency of HRD tumours, non-HRD tumours, HRD status not available for both GIS and tBRCA1/2 mutation, and the proportions of each category with GIS≥42, tBRCA1/2 and gBRCA1/2 mutations.

Of 37 cases, **29** (78%) had CRS1/2, and **8** (22%) had CRS 3.

Of **8** cases with CRS 3, **5** (63%) were HRD tumours (all (63%) had GIS≥42 with 2 (25%) concurrent tBRCA1/2 mutations and 1 (13%) coexistent gBRCA1/2 mutation). The **3** remaining cases (37%) with CRS 3 were non-HRD tumours.

Of **29** cases with CRS1/2, **16** (55%) were non-HRD tumours, **10** (35%) were HRD tumours with 6 concurrent gBRCA1/2 mutation, and **3** (10%) had no HRD status in which 2 had gBRCA1/2 mutation.

CRS categories	Total	HRD tumours	Non-HRD tumours	HRD status not available for both GIS and tBRCA1/2 mutation
CRS 1/2	29	10	16	3
CRS 3	8	5	3	0

Table 2: Frequency of HRD tumours, non-HRD tumours and HRD status not available for both GIS and tBRCA1/2 mutation according to their CRS categories.

CRS categories	HRD tumours	GIS≥42	tBRCA1/2 mutation	GIS≥42 and tBRCA 1/2 mutation	gBRCA1/2 mutation
CRS 1/2	10	7	7	4	6
CRS 3	5	5	2	2	1

Table 3: Frequency of HRD tumours according to their CRS and the proportions of each category with GIS≥42, tBRCA1/2 and gBRCA1/2 mutations.

Of 15 patients with HRD tumours, 5 (33%) showed a CRS 3. Of 9 patients with tBRCA1/2, 2 (22%) showed CRS 3. Of 12 patients with GIS≥42, 5 (42%) showed CRS 3. Of 9 patients with gBRCA1/2, 1 (11%) showed CRS 3.

Fisher's exact test (with significance level of P≤0.05), showed no significant correlation between CRS 3 and HRD tumours (**P=0.4172**), tBRCA1/2 mutation (**P=1.000**), GIS≥42 (**P=0.1904**) and gBRCA1/2 (**0.6847**).

Conclusions

HRD status predicts longer progression free survival.[6] CRS 3 demonstrates good response to NAC. A significant correlation between the two was not found in our small study. A larger study may be useful.

References:

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*Fisher's exact test calculation was performed using a free online calculator from website https://www.socscistatistics.com/