

THE UNCERTAIN BENEFIT OF ADJUVANT CHEMOTHERAPY IN ADVANCED LOW-GRADE SEROUS OVARIAN CANCER AND THE PIVOTAL ROLE OF SURGICAL CYTOREDUCTION.



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The question



Do low- and high-grade advanced ovarian tumours demonstrate a disparity in treatment characteristics and survival outcomes?

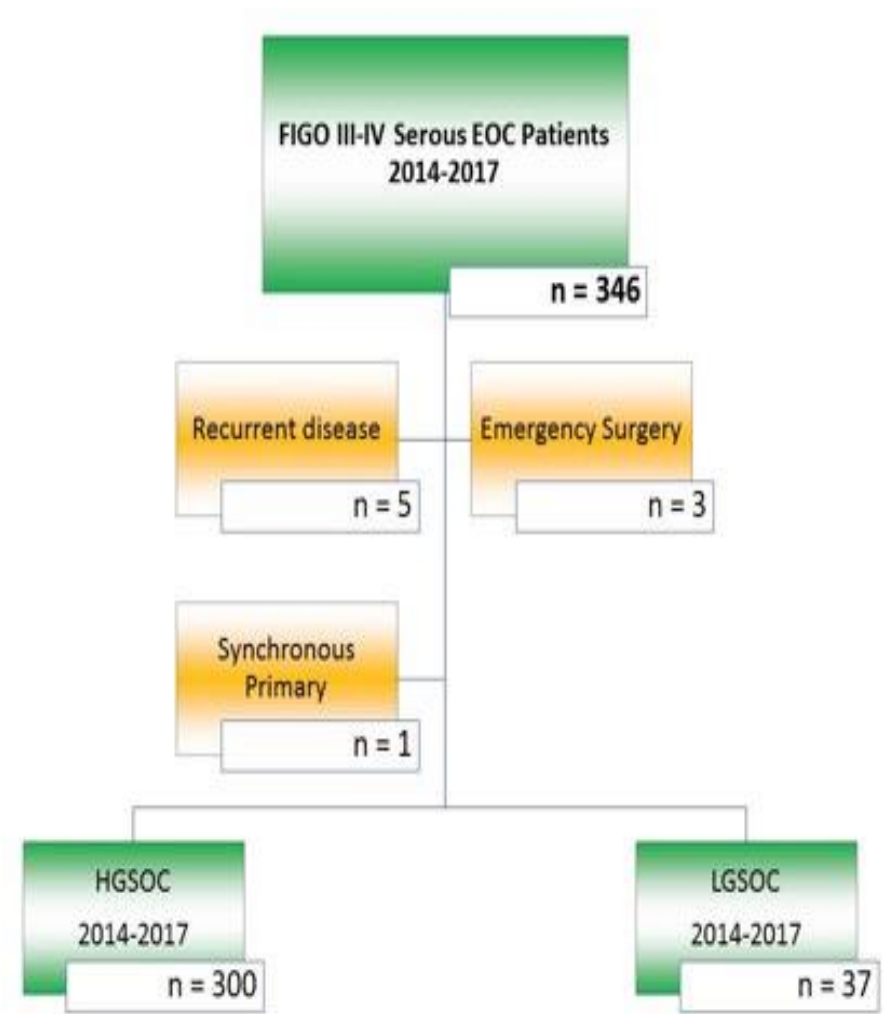
Why?



| Characteristics | LGSOC | HGSOC |
|-------------------------|---|--|
| Precursor lesion | Adenofibroma/cystadenoma → APST → non-inv MPSC → inv MPSC | STIC |
| Chromosomal instability | Low Low mitotic index | High High mitotic index |
| Genetic profile | KRAS BRAF ↑ ERBB2 | TP53 BRCA 1/2 ↓ |
| Hormonal profile | ER, PR expression | ER, PR expression |
| Progression | Indolent, step-wise | Rapid |
| Drug behavior | Extreme drug resistance to paclitaxel and carboplatin Favourable response to hormone therapy | Less frequent drug resistance to paclitaxel and carboplatin |

Vang, Russell et al. "Ovarian low-grade and high-grade serous carcinoma: pathogenesis, clinicopathologic and molecular biologic features, and diagnostic problems." *Advances in anatomic pathology* vol. 16,5 (2009): 267-82. doi:10.1097/PAP.0b013e3181b4fffa

METHODOLOGY



RESULTS

BASELINE CHARACTERISTICS



| | Low Grade Serous EOC 2014-2017 | High Grade Serous EOC 2014-2017 | P-value |
|--|--------------------------------|---------------------------------|----------|
| Patients | n = 37 | n = 300 | |
| Age (yrs) (Mean, SD) | 61.3 ± 10.9 | 63.9 ± 10.2 | 0.164 |
| Performance status (PS) | | | 0.419 |
| PS 0 | 20 (54.1%) | 124 (41.3%) | |
| PS 1 | 12 (32.4%) | 122 (40.7%) | |
| PS 2 | 3 (8.1%) | 42 (14.0%) | |
| PS 3 / 4 | 2 (5.4%) | 12 (4.0%) | |
| Pre-treatment CA125 (U/mL) (Median, Range) | 122 (25-9657) | 875 (13-28600) | < 0.0001 |
| Pre-treatment Cytology/Histology | | | |
| Cytology | 0 (0%) | 2 (0.7%) | |
| Biopsy | 37 (100%) | 298 (99.3%) | |
| Pre-Treatment CT | | | < 0.0001 |
| Calcified Deposits Present | 29 (78.4%) | 17 (5.7%) | |
| Absent Calcifications | 8 (21.6%) | 283 (94.3%) | |
| FIGO Stage | | | 0.478 |
| III A-B | 7 (11.9%) | 23 (13.9%) | |
| III C | 24 (62.1%) | 189 (58.8%) | |
| IV A-B | 6 (26.0%) | 88 (27.3%) | |

RESULTS

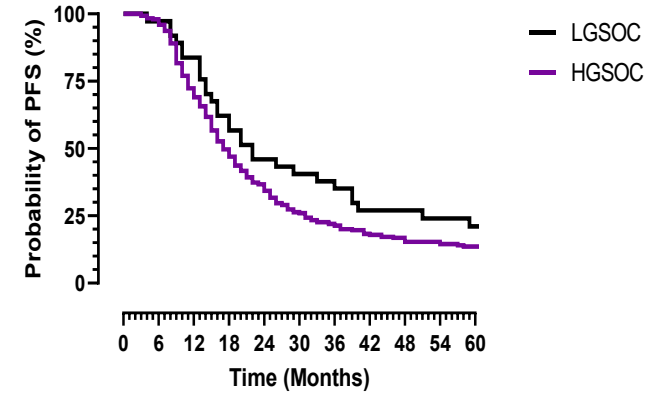
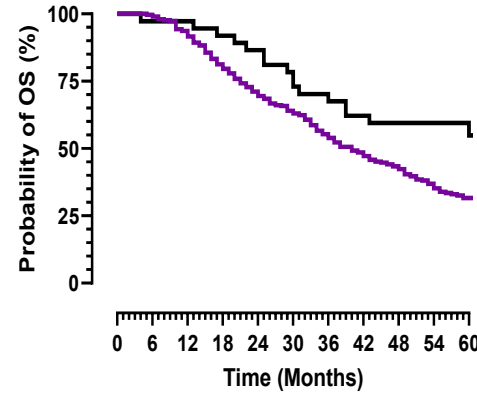
SURGICAL AND TREATMENT CHARACTERISTICS



| | Low-Grade Serous EOC n=37 | High-Grade Serous EOC n=300 | P-value |
|---|------------------------------|--------------------------------|----------|
| <i>Surgical setting</i> | | | |
| <i>Interval debulking surgery</i> | 13 (35.1%) | 240 (80.0%) | < 0.0001 |
| <i>Primary debulking surgery</i> | 24 (64.9%) | 60 (20.0%) | |
| <i>Peritoneal cancer index (PCI) (Median, Range)</i> | 8 (2-21) | 5 (1-24) | 0.0216 |
| <i>Cytoreduction Complete (CC 0-1)</i> | 17 (73%) | 264 (88.0%) | 0.8329 |
| <i>Incomplete (CC ≥ 2)</i> | 10 (27%) | 36 (12%) | |
| <i>Surgical Complexity Score (SCS) Low (1-3)</i> | 14 (37.8%) | 213 (71.0%) | < 0.0001 |
| <i>Intermediate (4-7)</i> | 20 (54%) | 74 (24.6%) | |
| <i>High (8-18)</i> | 3 (8.1%) | 13 (4.4%) | |
| <i>Adjuvant Treatment Platinum-based chemotherapy</i> | 10 (27 %) | 297 (99%) | < 0.0001 |
| <i>Other (Chemo-)Therapy</i> | 0 (0.0%) | 2 (0.7%) | |
| <i>No Adjuvant Treatment</i> | 27 (73%) | 1 (0.3%) | |

RESULTS

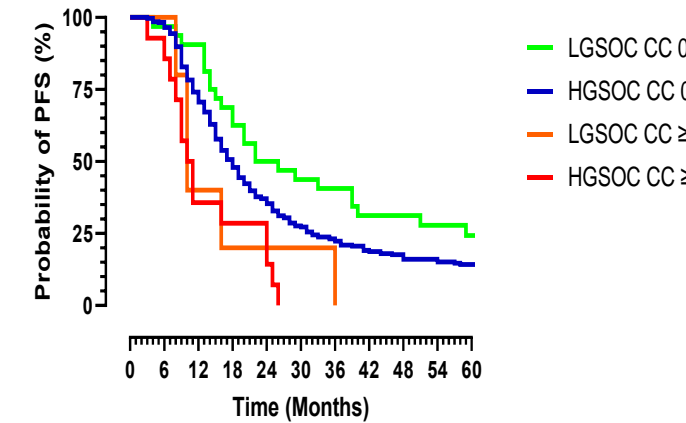
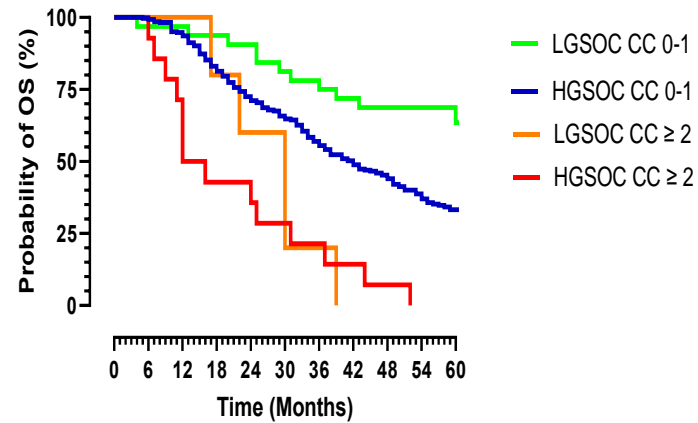
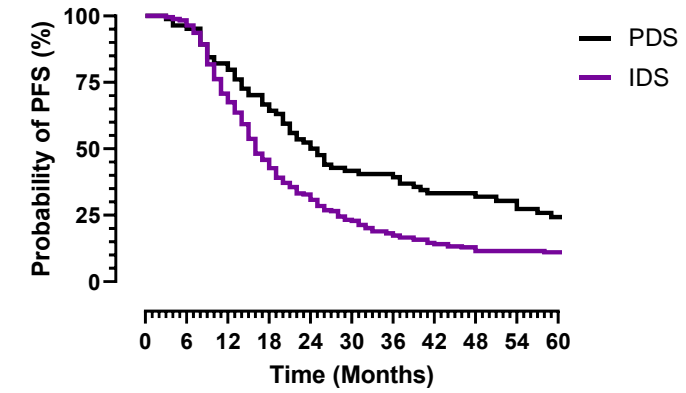
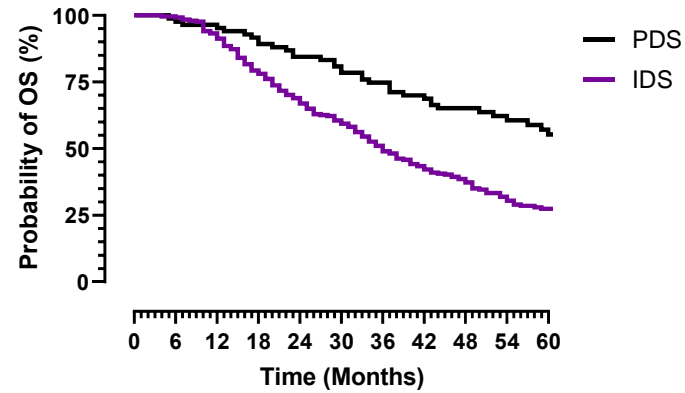
SURVIVAL ANALYSIS



| Survival 5-year | Whole cohort | LGSOC | HGSOC |
|--|-----------------------|---|-----------------------|
| OS % | 33% | 57% | 30% |
| OS median months with 95% confidence interval | 41 months (35.3-46.7) | Median not reached, mean 59.7months (50.5-69) | 40 months (34.6-45.4) |
| PFS % | 14% | 21.6% | 13% |
| PFS median months with 95% confidence interval | 16 months | 22 months (9.2-34.8) | 17 months (15.3-18.7) |

RESULTS

IMPACT OF SURGICAL APPROACH ON SURVIVAL OUTCOMES



Results

Multivariate analysis



| Covariates | Multivariate Analysis OS LGSOC | | | Multivariate Analysis OS HGSOC | | |
|----------------------------------|--------------------------------|------------------|------------------|--------------------------------|------------------|----------------|
| | HR | P | 95% CI | HR | P | 95% CI |
| FIGO stage | | | | | | |
| IIIa/b | 0.0001 | 0.9 | 0.0-1.1 | 0.9 | 0.83 | 0.38-2.2 |
| IIIc | 0.125 | 0.16 | 0.07-2.3 | 0.74 | 0.59 | 0.25-2.2 |
| IVa | 0.26 | 0.158 | 0.0-4.1 | 0.218 | 0.162 | 0.5-1.1 |
| IVb | 0.061 | 0.18 | 0.01-3.7 | 1.1 | 0.54 | 0.7-1.9 |
| Cytoreduction | | | | | | |
| Complete (CC 0-1) | 62.3 | <0.001 | 6.8-567.9 | 4.0 | <0.001 | 2.4-6.6 |
| Surgical complexity score | | | | | | |
| >4 | 5.3 | 0.024 | 1.2-22.8 | 0.88 | 0.56 | 0.6-1.3 |
| Surgical setting | | | | | | |
| Primary debulking | 3.2 | 0.16 | 0.6-16.6 | 1.8 | 0.017 | 1.1-2.9 |
| Clavien-dindo | | | | | | |
| 0/1 | 0.0001 | 0.93 | 0-.01-0.089 | 0.84 | 0.78 | 0.26-2.7 |
| 2 | 0.02 | 0.21 | 0.002-0.5 | 0.86 | 0.646 | 0.27-2.8 |
| 3 | 0.09 | 0.18 | 0.003-3 | 1.2 | 0.727 | 0.35-4.5 |
| 4 | 0.013 | 0.04 | 0.001-0.082 | - | - | - |

Discussion



LGSOC remains a disease that **primarily requires surgical treatment.**

No significant survival difference between our LGSOC patients who received adjuvant chemotherapy and those who did not.

Despite lack of adjuvant treatment in majority of LGSOC, their 5-year OS and PFS were approximately twice that of HGSOC patients.

LGSOC and HGSOC are different entities of serous EOC and consequently **deserve different management.** Therefore, we recommend **stratifying future studies** in EOC to these separate subtypes.

Limitations



THANK YOU FOR
LISTENING

QUESTIONS?



| | Low-Grade Serous EOC n=37 | High-Grade Serous EOC n=300 | P-value |
|---|------------------------------|--------------------------------|----------|
| <i>Operative time (minutes) (Mean, SD)</i> | 207 ± 93 | 150 ± 63 | < 0.0001 |
| <i>Intra-operative Blood Loss (cc) (Mean, SD)</i> | 632 ± 329 | 478 ± 323 | 0.0019 |
| <i>Post-operative Destination</i> | | | < 0.0001 |
| <i>Regular Ward</i> | 23 (62.2%) | 251 (83.7%) | |
| <i>HDU/ICU</i> | 9 (4.9%) | 72 (37.1%) | |
| <i>Length of Hospital Stay (days) (Median, Range)</i> | 9 (4-30) | 7 (3-68) | 0.0002 |
| <i>Peri-operative Morbidity (Clavien-Dindo)</i> | 27 (73.0%) | 280 (93.4%) | < 0.0001 |
| <i>0 - 2</i> | | | |
| <i>3 - 4</i> | 10 (27.0%) | 19 (6.3%) | |
| <i>5</i> | 0 (0.0%) | 1 (0.3%) | |