(R.R = 0.34, 95% CI: 0.13 – 0.88. Since HRV declines with age, we repeated the test with HRV/WBC in patients below 60 versus above 60. In this multivariate Cox regression, the ratio of (log)HRV/WBC tended to significantly predict Overall survival (OS) only in younger patients (O.R = 0.10, 95%CI: 0.01 – 1.27). We also confirmed association between cancer stage and survival only in women with low HRV but not in those with high HRV. ($X^2(1)$ = 4.08, 2.10, $p > 0.05$).

Conclusion We confirmed that higher HRV at diagnosis tended to significantly predict a better chance to survive. HRV/WBC ratio tended to significantly predict OS, but only in patients younger than 60 years old. The findings of our study suggest that vagal nerve activity, indexed by HRV, may be a new independent prognostic factor in ovarian cancer.

2022-RA-637-ESGO FIVE-YEAR UNIVERSAL TUMOR SCREENING OF *BRCA1/2* IN EPITHELIAL OVARIAN CARCINOMA;IS HISTOTYPE-DIRECTED HR-DEFICIENCY TESTING JUSTIFIED?

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Introduction/Background A popular dogma is that in epithelial ovarian carcinomas (EOCs) mutations in *BRCA1/2* and other homologous recombination (HR)-genes are exclusive to high-grade serous ovarian carcinomas (HGSOC). Nevertheless, the European guidelines recommend germline or tumor screening, regardless of histotype. Here, we report on the results of five-year prospective, universal 'tumor-first' screening of *BRCA1/2* and HR-genes in EOC and assess the relationship between identified mutations and histotypes.

Methodology EOCs were prospectively sequenced between September 2017 and December 2021 in two university medical centers in The Netherlands. The gene-panel included *BRCA1/2* and for a large subset of cases the panel was expanded with EOC-susceptibility HR-genes *BRIP1, PALB2, RAD51C* and *RAD51D*. All mutations (class 4 and 5 variants) were reported. Prior to sequencing, all EOC underwent a central pathology review by expert gynecopathologists.

Results The universal 'tumor-first' screening strategy was executed in the two centers on a total of 831 EOCs (table 1). In total, 73% were HGSOCs and 27% were EOC-cases of other histologies. The overall yield for *BRCA1/2* mutations in EOC was 13%, and the vast majority of mutations (94.5%) were identified in HGSOCs (yield of 17%; table 1). Intriguingly, 6/221 (2.7%) non-HGSOCs, i.e., n=3 high-grade endometroid, n=1 low-grade endometrioid and n=2 low-grade serous OC, harboured a *BRCA2* mutation. No *BRCA1/2* or HR-gene mutations were identified in clear cell and mucinous carcinomas. The results of extensive HRD testing of these six outliers will be presented at the meeting, including loss of heterozygosity, functional RAD51 assay and copy-number signatures.

Abstract 2022-RA-637-ESGO Table 1 Yield of BRCA1/2 and Homologous Recombination-Gene Mutations in Epithelial Ovarian Carcinoma

	BRCA1/2 mutations	*BRIP1, PALB2, RAD51C, RAD51D* mutations
	Center-1 and -2	Center-1
All EOC	13% (110/831)	1.9% (7/363)
HGSOC *	17% (104/610)	1.8% (5/271)
Other	2.7% (6/221)	2.2% (2/92)
EnOC – G3	16% (3/19)	0% (0/7)
EnOC – G1/2	2.9% (1/35)	0% (0/10)
LGSOC	3.4% (2/59)	4% (1/25)
CCC	0% (0/54)	0% (0/21)
MC	0% (0/31)	0% (0/16)
Carcinosarcoma	0% (0/12)	17% (1/6)
Other ¶	0% (0/11)	0% (0/7)

* 94.5% of all *BRCA1/2* mutations were detected in HGSOC.

¶ Including malignant Brenner tumor, mixed-type histology, mesonephric-like adenocarcinoma, undifferentiated carcinoma and small cell carcinoma.

HGSOC, high-grade serous ovarian carcinoma; LGSOC, low-grade serous ovarian carcinoma; EnOC, endometrioid ovarian carcinoma; G3, FIGO grade 3 (high-grade); G1/2, FIGO grade 1–2 (low-grade); CCC, clear cell carcinoma; MC, mucinous carcinoma.

Conclusion This large 'real-world' cohort of centrally revised and prospectively sequenced EOCs confirmed that *BRCA1/2* mutations are almost exclusively identified in HGSOC. Extensive HRD testing will inform us about the clinical relevance of the identified *BRCA1/2* and HR-gene mutations beyond HGSOCs and whether histotype-directed HRD-screening, after central pathology revision, may be justified.

2022-RA-643-ESGO MUCINOUS OVARIAN CANCERS – A SINGLE INSTITUTION ANALYSIS OF CLINICOPATHOLOGIC PROFILE AND SURVIVAL OUTCOMES

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Introduction/Background Mucinous ovarian carcinoma (MOC) is a rare subset of epithelial ovarian cancers. Prognosis of MOC is better in early stages, but worse in advanced stages owing to inadequate chemo-response. Literature is heavily dependent on small-sampled retrospective studies due to the rarity of this tumour. Hence, we embarked on this analysis of outcomes of MOC in an Indian tertiary-care cancer centre. The main objectives were to correlate clinicopathological factors associated with MOC; to characterise primary vs metastatic MOC; to assess role of appendicectomy and fertility-sparing surgery, and to analyse survival outcomes (progression-free survival – PFS and overall survival – OS).

Methodology Retrospective study of women diagnosed with MOC and treated from our tertiary-care cancer centre over a 10-year period; from January 2008 to December 2017. Patient records were reviewed, details assessed and data regarding recurrences and survival were analysed.

Results 109 patients were included in the study. Primary staging was done in 62%. 88% presented at stage I. 75% had primary ovarian mucinous histology, while 25% had metastatic histology. Metastatic MOC had absent borderline areas and advanced stage. 32% underwent appendicectomy, 2 cases had positive appendices and both were grossly abnormal. 23 patients recurred – 12 intraperitoneal, 8 extra-abdominal. Median follow-up of 49 months and 3-year PFS and OS were 70.2% and 77.9%. Early-stage MOC – median OS was not reached. Metastatic carcinomas had significantly poorer OS compared to advanced primary (10 vs 41 months p-<0.001). Fertility-sparing surgery with only ovarian cystectomy significantly reduced OS compared to adnexectomy.

Conclusion Of 109 MOCs, most had primary histology and early stage. Metastatic carcinoma had absent borderline areas, smaller size, bilaterality and advanced stage. Routine appendicectomy may not have a prognostic role. Factors affecting OS were the stage of disease and extent of surgery; not chemotherapy regime. Ovarian cystectomy alone resulted in poorer survival.

2022-RA-644-ESGO SURVIVAL IMPACT OF HISTOLOGICAL RESPONSE TO NEOADJUVANT CHEMOTHERAPY ACCORDING TO NUMBER OF CYCLES IN PATIENTS WITH ADVANCED OVARIAN CANCER

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Introduction/Background We sought to evaluate the impact of chemotherapy response score according to the number of cycles of neoadjuvant chemotherapy, on disease-free survival and overall survival, in patients with advanced epithelial ovarian cancer ineligible for primary debulking surgery.

Methodology Our multicenter retrospective study included patients with FIGO stage IIIC-IV epithelial ovarian cancer who underwent 3–4 or 6 cycles of a platinum and taxane-based neoadjuvant chemotherapy, followed by complete cytoreduction surgery (CC-0) or cytoreduction to minimal residual disease (CC-1), between January 2008 and December 2015, in four institutions. Disease-free survival and overall survival were assessed according to the histological response to chemotherapy defined by the validated chemotherapy response score.

Results A total of 365 patients were included: 219 (60.0%) received 3–4 cycles of neoadjuvant chemotherapy and 146 (40.0%) had 6 cycles of neoadjuvant chemotherapy before cytoreductive surgery. There were no significant differences in early relapses, disease-free survival and overall survival according to the number of neoadjuvant chemotherapy cycles. However, regardless of the number of neoadjuvant chemotherapy, persistent extensive histological disease (chemotherapy response score 1–2) was significantly associated with a higher peritoneal cancer index, minimal residual disease (CC-1) and early relapses. Median disease-free survival in patients with complete or near-complete response (score 3) was 28.3 months (95%CI [21.6–36.8]), whereas it was 16.3 months in patients with chemotherapy response score 1–2 (95%CI [14.7–18.0]), (p<0.001).

Conclusion In our cohort, the number of neoadjuvant chemotherapy cycles was not associated with disease-free survival or overall survival. Chemotherapy response score-3 improved oncological outcome regardless of the number of neoadjuvant chemotherapy cycles.

2022-RA-645-ESGO CONTRACEPTIVES AND CANCER RISKS IN *BRCA1/2* PATHOGENIC VARIANT CARRIERS, A SYSTEMATIC REVIEW AND META-ANALYSIS

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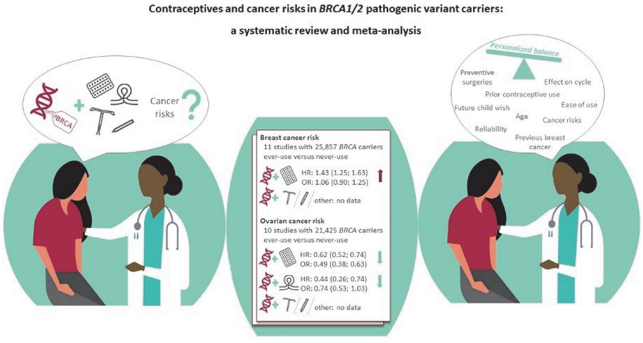
Introduction/Background *BRCA1*/2 pathogenic variant (PV) carriers have a high risk of breast and ovarian cancer. Contraceptives impact these risks in the general population. Among *BRCA1*/2-PV carriers, sufficient data and clear recommendations regarding contraceptives are lacking. We investigated how contraceptives modify breast and ovarian cancer risk in *BRCA1*/2-PV carriers.

Methodology We investigated the risk ratio for developing breast cancer or ovarian cancer in *BRCA1*/2-PV carriers who have used contraception (any kind) versus *BRCA1*/2-PV carriers who have not. A systematic search identified studies describing breast and/or ovarian cancer risk in *BRCA1*/2-PV carriers as modified by contraception. Random-effects meta-analyses were used to estimate pooled effects for breast and ovarian cancer risk separately. Subgroup analyses were conducted for *BRCA1* versus *BRCA2* and per contraceptive.



Abstract 2022-RA-645-ESGO Figure 1

Results Meta-analysis of 11 studies, including 25,857 women, reveals that breast cancer risk may be increased by the oral