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27 THERAPEUTIC ROLE OF PELVIC AND PARA-AORTIC LYMPHADENECTOMY IN APPARENT EARLY STAGE EPITHELIAL OVARIAN CANCER

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Introduction The therapeutic role of pelvic and para-aortic lymphadenectomy in surgical staging of apparent early-stage epithelial ovarian cancer (aeEOC) is still unclear. Recently, ESGO-ESMO consensus established that re-staging lymphadenectomy is not recommended if patients are already due to receive adjuvant chemotherapy for high-risk eEOC. The aim of this study was to evaluate the potential therapeutic role of systematic lymphadenectomy in patients with eEOC.

Methods Multi-center retrospective cohort study with CE approval, comparing women with aeEOC who underwent no lymphadenectomy (NL) versus lymph node sampling (SL) versus adequate systematic bilateral pelvic and para-aortic lymphadenectomy (AL) (defined as ≥20 lymph-nodes).

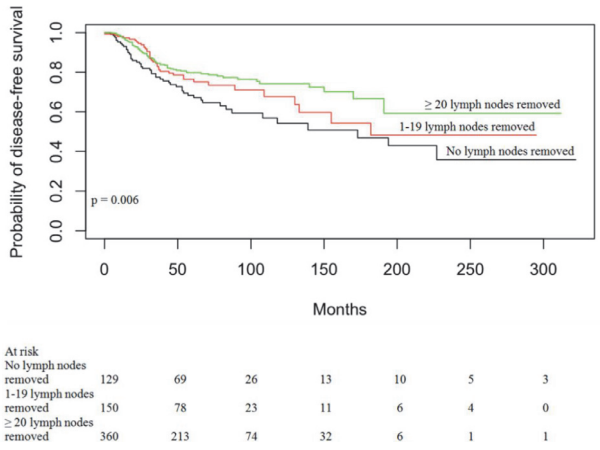
Inclusion criteria epithelial ovarian carcinoma; no bulky (≥10 mm short axis) pelvic or para-aortic lymph nodes at CT-scan; complete intra-peritoneal staging and at least 3 cycles of platinum-based adjuvant chemotherapy.

Results 639 of 2,559 patients with FIGO stage IA-IIIA1 ovarian cancer, met inclusion criteria. 360 (56.3%) underwent AL, 150 (23.5%) SL and 129 (20.2%) NL (table 1). AL patients were younger (p<0.001), experienced a higher number of grade 3–5 post-operative complications (p=0.008) and had a longer time to start chemotherapy (p=0.034). There was no difference in intra-operative complications. Median follow-up was 63 months (range, 5–342). The 5-year disease-free survival (DFS) was 79.7% vs. 76.5% vs. 68.3% (p=0.006) (figure 1), and 5-year overall survival (OS) was 92.3% vs. 94.5% vs. 89.8% (p=0.165) (figure 2) in women who received AL vs. SL vs. NL, respectively. Lymphadenectomy represented independent factor for DFS improvement, HR 0.52 (95%CI 0.37–0.73) (p<0.001).

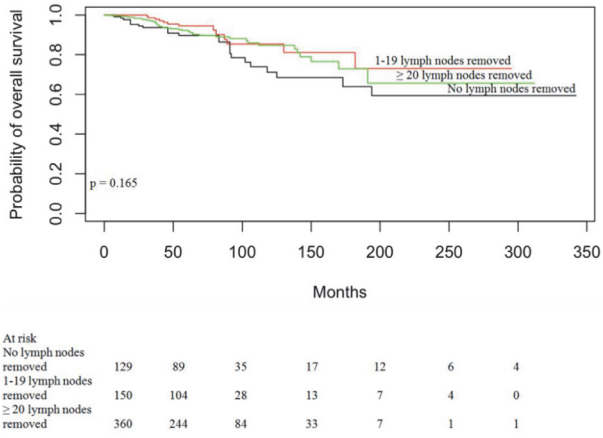
Abstract 27 Table 1 Patients' and surgery characteristics

Characteristics	All cases n = 639	Adequate lymphadenectomy (≥20 LN) n = 360	Lymph node sampling (1-19 LN) n = 150	No lymphadenectomy n = 129	p value
Mean age, years (+/- SD)	56 (+/- 11.3)	54 (+/- 10.6)	56 (+/-11.3)	60 (+/-12.1)	**<0.001**
Histology*					0.106
Serous	312 (48.8%)	172 (47.8%)	80 (53.3%)	60 (46.5%)	
Endometrioid	164 (25.7%)	100 (27.8%)	34 (22.7%)	30 (23.3%)	
Clear cell	105 (16.4%)	58 (16.1%)	28 (18.7%)	19 (14.7%)	
Indifferentiated	16 (2.5%)	7 (1.9%)	2 (1.3%)	7 (5.4%)	
Transitional	10 (1.6%)	7 (1.9%)	1 (0.7%)	2 (1.6%)	
Mixed	25 (3.9%)	13 (3.6%)	5 (3.3%)	7 (5.4%)	
Other	4 (0.6%)	1 (0.3%)	0 (0%)	3 (2.3%)	
Grade**					**0.025**
G1	35 (5.5%)	18 (5%)	3 (2%)	14 (10.9%)	
G2	145 (22.7%)	83 (23.1%)	33 (22%)	29 (22.5%)	
G3	456 (71.4%)	256 (71.1%)	114 (76%)	86 (66.7%)	
FIGO stage					**0.005**
IA	134 (21.0%)	68 (18.9%)	35 (23.3%)	31 (24.1%)	
IB	25 (3.9%)	16 (4.4%)	5 (3.3%)	4 (3.1%)	
IC1	137 (21.4%)	71 (19.7%)	37 (24.7%)	29 (22.5%)	
IC2	58 (9.1%)	34 (9.4%)	15 (10%)	9 (7.0%)	
IC3	43 (6.7%)	25 (7.0%)	7 (4.7%)	11 (8.6%)	
IIA	64 (10.0%)	36 (10%)	18 (12%)	10 (7.6%)	
IIB	120 (18.8%)	64 (17.8%)	21 (14%)	35 (27.1%)	
IIIA1	58 (9.1%)	46 (12.8%)	12 (8%)	0 (0%)	
Total number of lymph nodes removed, median (range)	32 (1-149)	48 (20-149)	11 (1-19)		**<0.001**
Median number of pelvic lymph nodes removed, (range)	18 (0-85)	28 (0-85)	5 (0-19)		**<0.001**
Median number of para-aortic lymph nodes removed, (range)	14 (0-82)	20.5 (0-82)	4 (0-19)		**<0.001**
Number of surgeries***					0.008
One	426 (66.7%)	229 (63.6%)	101 (67.3%)	96 (74.4%)	
Two (re-staging)	200 (31.3%)	128 (35.6%)	47 (31.3%)	25 (19.4%)	
Surgical approach at time of lymphadenectomy					**<0.001**
Laparotomy	368 (57.6%)	292 (81.1%)	76 (50.7%)		
Minimally-invasive	142 (22.2%)	68 (18.9%)	74 (49.3%)		
Number of patients with intra-operative complications	19 (3.0%)	12 (3.3%)	4 (2.7%)	3 (2.3%)	0.904
Number of patients with G3-5 early post-operative complications	27 (4.2%)	23 (6.4%)	2 (1.3%)	2 (1.6%)	**0.008**
Median time to start chemotherapy, days (range)*	36 (8-169)	36 (8-169)	39 (10-160)	33 (8-97)	**0.034**
Chemotherapy regimen					0.145
Carboplatin	237 (37.1%)	135 (37.5%)	47 (31.3%)	55 (42.6%)	
Carboplatin/Paclitaxel	402 (62.9%)	225 (62.5%)	103 (68.7%)	74 (57.4%)	

* 3 pts (0.5%) missing; ** 3 pts (0.4%) missing; *** 13 pts (2.0%) missing; * re-staging pts excluded and 44 pts missing.
LN: lymph nodes; SD: standard deviation; FIGO: International Federation of Gynecology and Obstetrics; LPT: laparotomy; G: grade



Abstract 27 Figure 1 Disease-free survival in patients undergoing adequate vs sampling vs no lymphadenectomy



Abstract 27 Figure 2 Overall survival in patients undergoing adequate vs sampling vs no lymphadenectomy

Conclusion Pelvic and para-aortic lymphadenectomy in surgical staging of eEOC improves DFS for the price of increasing post-operative complications and time to chemotherapy but does not affect OS.

IGCS20_1319

28 PREVALENCE AND PROGNOSIS OF LYNCH SYNDROME AND SPORADIC MISMATCH REPAIR DEFICIENCY IN THE COMBINED PORTEC-1,-2 AND -3 ENDOMETRIAL CANCER TRIALS

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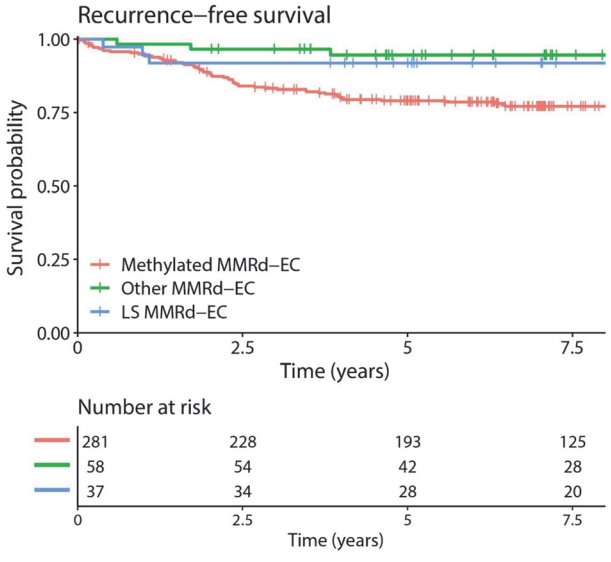
Introduction Here we aimed to evaluate the prevalence and prognosis of Lynch Syndrome (LS)-associated endometrial cancer (EC) in relation to sporadic mismatch repair deficient EC (MMRd-EC) in the combined PORTEC-1,-2 and 3 trials comprising 1336 ECs.

Methods MMR-status was determined by MMR-immunohistochemistry (MLH1/PMS2/MSH6/MSH2). MMRd-ECs with detected promoter hypermethylation of MLH1 were classified as sporadic (methylated MMRd-EC). For unmethylated MMRd-EC cases tumor and normal tissue next-generation sequencing was performed. ECs with MMR germline mutations were classified as LS-associated (LS MMRd-EC). Unmethylated MMRd-ECs without MMR germline mutations were classified as MMRd-EC due to other causes (other MMRd-EC). Overall and recurrence-free survival were estimated and compared using Kaplan-Meier method and pairwise log-rank test.

Results Among the 1336 ECs, 926 were MMR proficient. Of the 410 MMRd-EC, 376 could be fully triaged; 281 (75%) were methylated MMRd-ECs; 37 (10%) LS MMRd-ECs, and 58 (15%) other MMRd-ECs. The overall LS prevalence was 2.8%. Overall 5-year survival for LS MMRd-EC was 89% (95%CI 79–100%; p=0.055), other MMRd-EC 96% (92–100%; p=0.001), both compared to methylated MMRd-EC 79% (74–84%); 5-year recurrence-free survival was 92% (84–100%; p=0.123), 95% (89–100%; p=0.002), compared to 79% (74–84%), respectively.



Abstract 28 Figure 1 Kaplan-Meier survival curves for recurrence-freesurvival in the fully triaged MMRd patients

Conclusion The prevalence of LS in the PORTEC EC trial population was 3% and within the MMRd group 10%. LS MMRd-EC seems to have a better overall and recurrence-free survival than sporadic MMRd-EC caused by hypermethylation. Further research into the underlying causes of non-hypermethylated somatic MMRd-EC is ongoing.

IGCS20_1217

29 COMPREHENSIVE MOLECULAR ASSESSMENT OF MISMATCH REPAIR DEFICIENCY IN LYNCH-ASSOCIATED OVARIAN CANCERS USING NEXT-GENERATION SEQUENCING (NGS) PANEL

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Objectives Abnormalities in mismatch repair (MMR) gene may be the result of pathogenic germline (Lynch syndrome) and somatic mutations as well as epigenetic events. We aimed to examine the cause of MMR defects (MMRd) in non-serous/non-mucinous ovarian cancer (OC) through targeted mutational sequencing.

Methods Women with non-serous/mucinous OC (N = 215) were prospectively recruited from three cancer centers in Ontario, Canada. Tumors were assessed for MMR protein expression by immunohistochemistry. Matched MMRd tumor-normal samples were run on a custom NGS panel to identify germline and somatic mutations, copy number variants, rearrangements and promoter methylation in MMR and associated genes.

Results Of 215 women enrolled in our study, 185 (86%) had OC and 30 (14%) had synchronous OC and endometrial cancer. Twenty-eight (13%) cases were MMRd, 11 of which were synchronous. Using the NGS panel, Lynch syndrome (LS) was detected in 39% of MMRd cases (11/28; 7 OC and 4 synchronous): 7 MSH6, 2 MLH1, 1 PMS2, and 1 MSH2. An explanation for the observed MMR phenotype was available for 18/20 deficient cases, including 9/10 MLH1-/PMS2- (7 somatic methylation, 1 bi-allelic somatic deletion, 1 germline mutation), 0/1 PMS2-, 6/7 MSH6- (6 germline mutations) and 2/2 MSH2-/MSH6- (1 germline mutation, 1 bi-allelic somatic mutation). Concordance between clinical and research panel sequencing results was 90%.

Conclusions Use of our custom NGS panel allows for the streamlined assessment of hereditary and somatic causes of MMR deficiency in OC and may be an attractive screening strategy for LS in this population.