Methodology Expression analysis of NR2F6 in 142 endometrial cancer patients was performed by immunohistochemistry. Staining intensity of tumor cells was computerized assessed semi-quantitatively, and results were correlated with clinicopathological characteristics and survival.
Results 46 of 117 evaluable samples (39.3%) showed an overexpression of NR2F6, leading to an improvement of the overall (OS) and disease-free survival (DFS). In NR2F6 positive patients, the mean OS was 156.6 months (95% confidence interval (CI): 142.4 – 170.8) compared to 105.8 months in NR2F6 negative patients (95% CI: 85.6 – 125.9; $p = 0.025$). The disease-free survival differed by 58.4 months (156 months (95% CI: 142.2 – 169.9) vs. 97.6 months (95% CI: 74.7 – 120.6), $p = 0.004$). Furthermore, we found significant associations between NR2F6 positivity, MMR status, and PD1 status. A multivariate analysis suggests NR2F6 to be an independent factor influencing the disease-free survival ($p = 0.037$).
Conclusion This is the first report on the prognostic impact of NR2F6 in endometrial cancer patients. We could demonstrate that there is a significant better progression-free and overall survival for patients with overexpression of NR2F6 in patients with endometrial cancer. Further studies are required to validate its prognostic impact.

2022-RA-1345-ESGO WHEN ENDOMETRIAL CANCER SPARES NO AGE

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Introduction/Background Endometrial cancer (EC) is a postmenopausal disease and occurs in only 4% of women 40 years and below.[1]Patients in this age group present with a low grade EC with excellent prognosis.[2] Because of this age group, fertility sparing approach is a reasonable option for selected patients and must be tackled. This paper aims to share this unusual case in the medical field with the hope of being able to contribute with the establishment of a consensus on the management of EC in the young, that is fertility preserving.
Methodology KE is a 36 year old Gravida 0 with primary infertility, complaining of menorrhagia. She has a body mass index of 31.9 kg/m^2. Ultrasound was done which showed thickened endometrium, hyperechoic with cystic spaces measuring 1.8 cm. Sampling was done which showed Endometrioid Adenocarcinoma. Abdominal CT scan showed a non enhancing unilocular, cystic mass measuring 3.5 x 2.5 cm, on the left ovary. No discrete uterine nor abdominopelvic mass, nor lymphadenopathy. She underwent Exploratory Laparotomy, Extrafascial Hysterectomy, with evaluation of lymph nodes. Her histopathology results confirmed diagnosis.
Results EC develops due to unopposed estrogen exposure. Risk factors include obesity, nulliparity, early menarche, polycystic ovarian syndrome, and sequential use of contraception.[4] The standard treatment for EC is surgery. However, in some parts of the world, medical treatment is being applied with the most common regimen consisting of medroxyprogesterone acetate at 50 to 600 mg daily and megestrol acetate at 160 mg daily.[1] Hormonal treatment has been shown to be successful in patients with a FIGO 1A staging.[5] Factors to consider when doing conservative management include grade of disease, depth of myometrial invasion, presence of adnexal masses, and their future child bearing plans.[3]
Conclusion A consensus on a fertility sparing treatment should be made for young patients with EC.

2022-RA-1346-ESGO PREDICTIVE FACTORS FOR ADNEXAL INVOLVEMENT IN ENDOMETRIAL CANCER, WITH A FOCUS ON FIGO STAGE IIIA, AN UNCOMMON ENTITY

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Introduction/Background To assess the incidence of endometrial cancer (EC) FIGO stage IIIA, and evaluate predictors of adnexal involvement, and its role as prognostic factor of recurrence and death in EC.
Methodology Records of all consecutive EC patients who underwent primary surgery between January 2005 and November 2021 at Fondazione Policlinico A. Gemelli, Rome, were retrospectively reviewed. Potential predictive factors of adnexal involvement were assessed by logistic regression models. Overall survival (OS) and recurrence-free survival (RFS) were estimated using Kaplan-Meier method and potential independent prognostic factors assessed by Cox proportional-hazard models.

Abstract 2022-RA-1346-ESGO Table 1

		Univariable Analysis Adnexal Involvement		Multivariable Analysis
	Yes (n=207)	No (n=1872)	OR (95% CI); p	OR (95% CI); p
Age at diagnosis	63.0 (54.0-70.5)	62.0 (55.0-70.0)	1.00 (0.99; 1.01); 0.772	
BMI	26.7 (22.7-31.2)	28.5 (24.2-33.7)	**0.96 (0.94; 0.98); 0.001**	**0.96 (0.94; 0.99); 0.004**
Menopause	168 (81.2)	1565 (83.6)	0.85 (0.58; 1.22); 0.371	
Expressed Molecular Markers				
Beta-catenin	14 (6.8)	220 (11.8)	**0.54 (0.31; 0.95); 0.034**	**0.41 (0.21; 0.79); 0.008**
ER	140 (67.6)	1115 (59.6)	**1.42 (1.04; 1.92); 0.025**	**10.05 (1.45; 69.57); 0.019**
PR	138 (66.7)	1115 (59.6)	**1.36 (1.00; 1.84); 0.048**	*0.16 (0.02; 1.14); 0.067*
*iMMR phenotype**	115 (55.6)	908 (48.5)	*1.33 (0.99; 1.77); 0.055*	**1.96 (1.24; 3.08); 0.004**
P53	91 (44.0)	225 (12.0)	**5.74 (4.22; 7.81); <0.001**	*1.73 (0.95; 3.13); 0.071*
Histology				
Endometrioid histotype	107 (51.7)	1531 (81.8)	**0.24 (0.18; 0.32); <0.001**	*0.55 (0.30; 1.01); 0.052*
FIGO Grade				
G1	1 (0.5)	313 (17.3)	**0.01 (0.00; 0.08); <0.001**	**0.07 (0.01; 0.53); 0.010**
G2	65 (31.4)	1030 (56.9)	**0.21 (0.15; 0.28); <0.001**	*0.65 (0.42; 1.02); 0.059*
G3 (Ref.)	141 (68.1)	466 (25.8)	-	-
Tumor size >20mm	186 (89.9)	1294 (69.1)	**3.96 (2.49; 6.28); <0.001**	*1.58 (0.92; 2.72); 0.093*
Tumor size, mm	50.0 (36.2-70.0)	35.0 (23.0-40.0)	**1.03 (1.03; 1.04); <0.001**	
Myometrial Infiltration >50%	146 (70.5)	636 (34.0)	**4.65 (3.40; 6.37); <0.001**	**1.51 (1.03; 2.21); 0.035**
LVSI				
None (Ref.)	73 (35.3)	1409 (75.3)	-	-
Isolated	44 (21.3)	219 (11.7)	**3.88 (2.60; 5.79); <0.001**	**2.51 (1.59; 3.97); <0.001**
Diffuse	90 (43.5)	244 (13.0)	**7.12 (5.08; 9.97); <0.001**	**3.27 (2.16; 4.94); <0.001**
Cervical Stromal Invasion	104 (50.2)	195 (10.4)	**8.68 (6.37; 11.84); <0.001**	**4.26 (3.00; 6.05); <0.001**

Abbreviations: BMI: Body Mass Index; ER: estrogen receptor; PR: progesterone receptor; iMMR: instable Mismatch Repair; FIGO: International Federation of Gynecology and Obstetrics; LVSI: Lymphovascular space invasion; VB: Vaginal Brachytherapy; EBRT: External beam Radiation Therapy; OR: Odd Ratio; CI: confidence interval
* Immune-phenotype includes all Mismatch Repair System Components expression, i.e. MLH1: Murl. Homolog 1; MSH2: MutS homolog 2; MSH6: MutS homolog 6 gene, and PMS2: PMS1 Homolog 2.
** Data are expressed as absolute and percentage frequencies if qualitative, as median and interquartile range (IQR) if quantitative. In **bold** significant findings (p<0.05); in *italic* suggestive associations (0.1<p<0.05).

Results 2079 patients were finally included in the study. Of those, 55 were stage IIIA EC (annual incidence 0.11%). Recurrences occurred in 16 out of 55 patients (29.1%), mostly pelvic and lymphatic (43.8% each). Notably, 27/39 (69.2%) who did not recur underwent chemotherapy with external beam radiation therapy. 5-years RFS and OS in stage IIIA were 72.7% and 85.5%, respectively.Overall, 207 patients had adnexal involvement (annual incidence 0.42%), with myometrial infiltration [(MI) OR 1.51, 95% 1.03–2.21; 0.035],

isolated and diffuse lymphovascular space invasion [(LVSI) OR 2.51, 95%CI 1.59–3.97; OR 3.27, 95%CI 2.16–4.94; p<0.001, respectively), cervical stromal invasion [(CSI) OR 4.26, 95%CI 3.00–6.05; p<0.001], and instable mismatch repair (iMMR) phenotype (OR 1.96, 95%CI 1.24–3.08; p=0.004) found as independent predictors (Table). Remarkably, adnexal involvement in EC further revealed an independent negative predictive factor of RFS (HR 3.20, 95%CI 1.66–6.18; p=0.001), whilst only a suggestive negative role emerged on OS (HR 1.73, 95%CI 0.93–3.24; p=0.086). Consistently, 5-years RFS and OS were shorter among women with adnexal involvement compared with those without (63.3 vs. 87.5%, and 68.6 vs. 92.9%, p<0.001, respectively).

Conclusion Main predictors of adnexal involvement in EC are iMMR phenotype, MI, isolated and diffuse LVSI, and CSI. Although adnexal involvement incidence is low, this may be associated with higher recurrence risk.

2022-RA-1357-ESGO FACTORS ASSOCIATED WITH AN INCREASED RISK OF RECURRENCE IN ENDOMETRIAL CANCER PATIENTS: A RETROSPECTIVE COHORT STUDY

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Introduction/Background The aim of this study was to identify clinical and pathologic factors associated with the risk of recurrence in patients with endometrial cancer (EC).

Methodology We included patients who underwent surgery for EC in our institution between 2007 and 2019. Data on demographic characteristics, surgery and pathology reports, adjuvant treatment and follow-up was collected from electronic patient files. Patients were divided into two groups: recurrence and no recurrence. Clinical and pathologic factors were compared using Student T-test, Chi-square or Fisher's exact test. Univariate and multivariate Cox-proportional hazard models were used to assess the impact of the evaluated factors on the risk of recurrence.

Results In total 286 patients were included in the analysis. In a mean follow-up time of 59 months, EC recurrence was diagnosed in 60 (20.9%) patients, 75% of which were diagnosed in the first 24 months after surgery. Compared to patients with no recurrence, patients with recurrent EC had more frequently type II (56.7%vs.25.2%), high-grade (61.7% vs.32.7%), stage III-IV tumors (35%vs.17.3%), tumor>2 cm (95%vs.78.8%), myometrial infiltration>50% (48.3%vs.29.2%) and lympho-vascular space invasion (LVSI; 60.9%vs.25.8%). Lymphadenectomy had been indicated more often in patients with recurrent EC (71.7%vs.44.2%), however, there was no association between performance of lymphadenectomy and EC recurrence. In univariate survival analysis, risk of recurrence was higher in patients with type II (HR:4.12;*p<0.001*), high-grade tumors (HR:3.06;*p<0.001*), tumor>2 cm (HR:4.93; *p=0.007*), myometrial infiltration>50% (HR:2.43;*p=0.001*), cervix infiltration (HR:2.29;*p<0.001*), adnexal tumor (HR:1.97;*p=0.031*), LVSI (HR:4.39,*p=0.001*) and stage IV (HR:6.85;*p<0.001*). In multivariate analysis, only LVSI remained significantly associated with an increased risk of recurrence (HR:5.36;*p=0.017*).

Conclusion LVSI is an independent risk factor for EC recurrence, while performing lymphadenectomy had no impact on the risk of recurrence. Identifying patients with a higher risk of EC recurrence is important in order to concentrate follow-up efforts on patients who can benefit the most from it.

2022-RA-1364-ESGO IMPLEMENTATION OF MOLECULAR CLASSIFICATION IN ENDOMETRIAL CANCER AND ITS IMPACT ON INDICATION OF ADJUVANT THERAPY

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Introduction/Background Adjuvant treatment in endometrial carcinoma was based on classical risk stratification which included clinicopathological data. Molecular classification has been recently incorporated into risk stratification by ESGO guidelines. The aim of this study is to describe the distribution of molecular groups in our population and to evaluate its impact on indication of adjuvant treatment.

Methodology Retrospective cohort study including all newly endometrial cancer cases diagnosed between January 2021 and April 2022 with available molecular data. Immunochemistry for TP53 and MMR proteins and Sanger sequencing for POLE mutations were done on diagnostic biopsy tissue. Risk stratification and indication of adjuvant therapy followed new histomolecular groups.

Results 66 cases were included. Table 1 shows clinicopathological data.

Abstract 2022-RA-1364-ESGO Table 1 Clinicopathological data

Hystotype	N	%
Endometrioid	49	74.2
Serous carcinoma	8	12.1
Clear-cell	1	1.5
Carcinosarcoma	6	9.1
Undifferenciated	2	3
Grade		
G1	21	31.8
G2	21	31.8
G3	24	36.4
FIGO stage		
I	51	77.3
II	4	6.1
III	4	6.1
IV	4	6.1